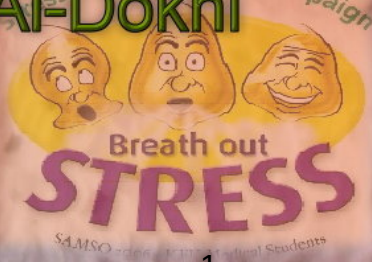
SMSO

Clinical Pediatric By 15 Students

Edited by:
Hussain Al-Baharna & Mohammad Al-Dokhi



2006-2007

15 STUDENTS

1- Hussain Al-Baharna
2- Ibrahim Al-Jabr
3- Akeel Al-Haiz
4- Jawad Al-Habdan
5- Mazen Al-Aithan
6- Mohammad Al-Sultan
7- Ibrahim Al-Kazim
8- Ibrahim Al-Sayeq
9- Moneer Abu-Kabbos
10- Ammar Abu-Zohairah
11- Abdulaziz Al-Qamdi
12- Faisal AL-Hawaj
13- Khalid Al-Efraij
14- Ahmad Al-Sakka
15- Mohammad Al-Dokhi

Fluid and electrolytes

cc = cubic centimeter = milliliter
All the concentrations of fluids given to the patients can be (and they usually) little more or less than the calculated numbers (approximations) because companies prepare fluids with specific concentrations, and we choose the most appropriate one.

✓ **Maintenance fluid**

Amount needed every day (for compensation and to burn calories)
It includes sensible and insensible water loss
Sensible: e.g. urine and stools
Insensible: e.g. respiration (evaporation) and sweating

We calculate it by any of the two methods below:

(1) The first method:

First 10 kg → 100 cc/Kg
Second 10 kg → 50 cc/Kg
For any one kg above 20 → 20 cc/KG

For example: child with 20 kg weight, we give him 1500 cc. For first 10 kg we give him 100 cc/kg, so we give him a total of 1000 cc for the first 10 kg of his weight. For the rest, which is 10kg (20-10=10kg) we give him 50cc/kg, so we will give him 500cc for the second 10kg. The total will be 1500cc (1.5L) for the 20 kg.
Another example: 37 kg → we give him 1840cc
As in previous example, first 10 kg →1000cc
Second 10 kg → 500 cc
Then we will have 17kg (37-20=17kg). From the rule, for any single kg after 20kg → we give 20 cc/kg. So, for the 17 kg → 17 X 20 = 340 ml. The total will be 340cc+1500cc=1840cc
Another example: 45 kg child → 2000cc

(2)The second method:

Is by using the surface area to calculate the maintenance fluid. This method is rarely used and we don' t use it usually.

Maintenance fluid =1600cc/m2/day

✓ Types of fluids

We have special fluids used in rehydration. For example, we don' t use tape water, because it is non-sterile and its tonicity (osmolality) is unknown. Also, we don' t use distilled water because it is hypotonic fluid and will cause swelling and then rupture of the RBCs (hemolysis).
The most important factor in determining the fluid type is sodium concentration in the fluid.
Sodium requirement by the body is 2-4 meq/kg/day. We give usually the upper limit in all cases (4 meq/kg/day)

Examples:
Example no 1: 20 kg child → needs maintenance fluid of 1500cc/day and 80 meq sodium/day.
Example no 2: 37kg child → needs maintenance of 1840cc (we make it 2000cc for easy administration and calculation) and 148 meq sodium/day
Example no 3: 45kg child → 2000cc and 180 meq sodium/day.

There are four types of fluids that concern us in pediatrics which are:
Normal saline with sodium concentration of 154 meq/L
1/2 normal saline with sodium concentration of 77 meq/L
1/4 normal saline with sodium concentration of 39 meq/L
Ringer's lactate with sodium concentration of 131 meq/l (but ringers lactate is not used very much because of different concentrations of other ions, it is usually used in surgery)

In example no 1, we said we need to give the patient 1500cc/day and 80 meq sodium/day. The problem is that fluid bottles come with specific volumes (for example 250cc, 500cc, 1 liter). In this patient, we can give 1 bottle of 1 liter and another bottle of 500cc because we don' t have bottles of 1.5 liter. But we have to know which type of fluid to give. And since the patient needs 1500cc and 80 meq/day →this means that the fluid to be given should have sodium concentration of 80 meq/1500cc, and as we said no 1500cc bottles, so, we calculate the concentration in one liter → it will be equal to 53.33 meq/l (equal to 26.665 meq Na/500cc) the fluid which is most appropriate for this patient is 1/4 normal saline

because its concentration is the nearest concentration to the patient need (53.33meq/l and 39meq/l)
In example 2: we give 1/2 normal saline
In example 3: we give 1/2 normal saline

We have simple rule to know the fluid needed instead of all these calculations.
For any child: =<20 kg → give 1/4 normal saline
For any child: >20 kg → give 1/2 normal saline

✓ Additives

We can't give the patient fluid with only sodium for 24 hours. We have to add dextrose and potassium.
We add D5 (5% dextrose) which means 5 gram glucose in 100cc.
Potassium requirement is 1-2 meq/kg/day. Here in potassium, we usually give the lower limit (1 meq/kg/day) because hyperkalemia is a real emergency and very dangerous (it causes arrhythmia and asystole). So, we should avoid hyperkalemia and give the patient lower limit. In contrast, we give the upper limit of sodium as we mentioned before, because hypernatremia is less common and not as dangerous as hyperkalemia.
Now, back to our examples,
20kg child needs 20 meq potasium/day. And he needs as we said before 1500cc. in one liter, the concentration of potassium will be 13.33

Rate of fluid administration (@) = amount of fluid to be given/24 hours

In writing order for the nurse, we write it like this:
D5 1/4 nl sal. @ 60ml/hr with 10 meqK/L (approximately 60ml)

Example: 33 kg child
Fluid: 1760cc
Sodium:132 meq Na/day
The fluid type is 1/2 nl sal because: 132/1760 X 1000=75meq/L
Additives: D5 and K (33meq but in one liter →
33/1760X1000=18.75 which is almost equal to 20

So the order is
D5 1/2 nl sal @ 70cc/hr with 20 meqK/L

✓ Dehydration

It is one of the most common problems in pediatrics.

- Classification: according to either

  1-Tonicity: isotonic (serum Na is between 130 and 150 meq/l), hypertonic (>150) or hypotonic (<130) dehydration. Commonest is isotonic (85% of cases). Hypertonic is seen in 10% of cases. Hypotonic is the least with only 5%. Usually, we don' t use this method because we always consider any case of dehydration (in general) as isotonic dehydration.

  2-Severitiy: the usual classification. Dehydration is classified into mild, moderate or severe dehydration depending on history and physical examination (so, it is mostly subjective with some variation from one doctor to another).
  There is a nice table in nelson, fifth edition, page 162, table 33-5 and it is copied below.

TABLE 33–5. Assessment of Degree of Dehydration

	Mild	Moderate	Severe
Infant	5%	10%	15%
Adolescent	3%	6%	9%
Infants and young children	Thirsty; alert; restless	Thirsty; restless or lethargic but irritable or drowsy	Drowsy; limp cold, sweaty, cyanotic extremities; may be comatose
Older children	Thirsty; alert; restless	Thirsty; alert (usually)	Usually conscious (but at reduced level), apprehensive; cold, sweaty, cyanotic extremities, wrinkled skin on fingers and toes; muscle cramps
Signs and Symptoms			
Tachycardia	Absent	Present	Present
Palpable pulses	Present	Present (weak)	Decreased
Blood pressure	Normal	Orthostatic hypotension	Hypotension
Cutaneous perfusion	Normal	Normal	Reduced and mottled
Skin turgor	Normal	Slight reduction	Reduced
Fontanel	Normal	Slightly depressed	Sunken
Mucous membrane	Moist	Dry	Very dry
Tears	Present	Present or absent	Absent
Respirations	Normal	Deep, may be rapid	Deep and rapid
Urine output	Normal	Oliguria	Anuria and severe oliguria

Data from World Health Organization.

Dr.kamaleddin gave another classification. He said for patients of 3 years and below: 5 to 9 % body weight loss is mild, 10 to 14% is moderate and 15% and above is severe. For those above 3 years: 3 to 5% is mild, 6 to 8% is moderate, 9% and above is severe.

- Management

In the management, we give the deficit volume + maintenance volume + ongoing loss (ongoing loss: we calculate it directly, for example if the patient has diarrhea, we calculate the volume of diarrhea each time the patient go to toilet or after changing the diaper and we give the patient same amount)

For the deficit volume, we have to assess the patient and determine the severity of dehydration, and according to that we give the deficit volume. For example, if the patient has mild dehydration (5%) and he is 25 kg we give
50 (5% means 50 ml /kg) X 25 (the weight) = 1250cc + 1600cc (the maintenance) = 2850 which is almost 3 liters

There are specific indications of giving the fluid as bolus, for example tachycardia, hypotension and weak pulse. The bolus fluid is always normal saline regardless of sodium need by the patient (not any other fluid, always normal saline), this is because normal saline tonicity is high and it stays inside vessels, so it raises intravascular volume and normalizes blood pressure rapidly. If there is indication for bolus, we give
10-20 cc/kg (as bolus) and subtract it from the total volume. For example, in our 25 kg patient, if we give 20cc/kg as bolus, this means we will give him 500cc bolus. Then, we subtract it from the total volume (3000cc - 500cc = 2500cc). If the patient didn't improve after the bolus dose, we can give second bolus and here we do just as with first bolus (subtract it from total). The rest of fluid after the bolus dose, we give it as continuous infusion for 24 hours. Sometimes, the patient improves after the bolus dose but not totally, here we can give half of the ***deficit volume only*** in 8 hours (this means 1250X 1/2 = 625cc in 8 hours → 80cc/hr + 70cc/hr (for maintenance) so, 150cc/hr in first 8 hours) and the other half in 16 hours (625cc in 16 hrs → 40cc/hr + 70cc/hr → total of 110cc/hr for the next 16 hrs.

In hypertonic dehydration it is very important ***not*** to give the deficit volume rapidly. We try to give it in two days or even more. This is because of high risk of developing cerebral edema if we give the fluid in single day.

Ideal rehydration in all patients with mild or moderate dehydration is oral rehydration salts -ORS- (Na = 90meq/l, K = 20meq/l) because it is cheep, can be made at home and no need for IV. We give ORS in frequent and small doses. In sever dehydration, we give IV fluids.
Vomiting is ***not*** contraindication of oral rehydration.
Vomiting in gastroenteritis is due to acidosis, once we give bicarbonate, vomiting subsides.

Nephrotic syndrome

- **Def.:** the characteristic features of nephrotic syndrome "N.S." are:
  1. Heavy proteinuria.
  2. hypoalbuminemia
  3. edema
  4. hyperlipidemia

- **Proteinuria:**

Obtained by 24 h. urine collection: these are for child
>50 mg/kg/d.
>40 mg/m^2/h.
>1 g/m^2/d.
For adult >3.5 g/d.

Methods of measuring proteinuria:

1. 24h urine collection
2. simple urine analysis
3. spots protein to creatinine ratio " most accurate one"

24h urine collection:

Whenever you do 24 h urine collection you have to check for:

a. Volume.
b. Protein
c. Creatinine excretion

For adequacy of collection -b/c volume of urine not measure adequacy of collection but it measures how much you drink- creatinine excretion should be done.
Normal creatinine excretion:
For male: 15-20mg/kg/d
Female: 12-15mg/kg/d
Child: up to 10 mg/kg/d
So, if u do 24hs urine collection, 1st calculate creatinine excretion:

- If it is within normal range then looks to protein and consider it as appropriate sample.
- If u get too mush creatinine this means over collected for more than day
- If u get too less creatinine this means under collected for less than 24hs

Note: 24h urine collection may not easy to be done in child.

Simple urine analysis;

Dipstick by color change "colorimetric"
Normal protein excretion 100-150mg/d
Grades:

1. 30mg/d
2. 30-100mg/d
3. 300-500mg/d
4. >500mg/d - 2g/d: definitive N.S. but still we can't sure.

***Spots protein to creatinine* ratio** "most accurate one"

Normal <0.2
N.S. if >2-4

- **Hypoalbuminemia:**

<2.5g/dl serum albumin

- **Edema:**

Urinary protein loss leads to hypoalbuminemia, which causes a decrease in the plasma oncotic pressure and transudation of fluid from the intravascular compartment to the interstitial space. The reduction in intravascular volume decreases renal perfusion pressure, activating the renin-angiotensin-aldosterone system, which stimulates tubular reabsorption of Na. The reduced intravascular volume also stimulates the release of ADH, which enhances the reabsorption of H_2O in the collecting duct. Because of the decreased plasma oncotic pressure, fluid shifts into the interstitial space, exacerbating the edema.

Could be just periorbital or pedal "sacral"
Or more sever anasarca or generalize body edema.

- **Hyperlipidemia:**

>200mg/dl.
Due to two reasons:

1. Loss of lipoprotein lipase b/c. it is an enzyme which is protein.

   Decrease of this enzyme level in plasma lead to decrease lipid metabolism.
2. hypoalbuminemia stimulate generalized hepatic synthesis including lipoprotein

- **Classification of N.S.:**
  1. idiopathic "90% " :
     a. minimal change nephrotic syndrome 85%
     b. focal segmental glomerulosclerosis 10%
     c. mesangial proliferation 5%
  2. 2ry to membranous nephropathy, membranous proliferative GN, lupus, Henoch Schonlein purpura, HBV, HCV, HIV…
  3. Congenital e.g. Finnish syndrome "AR"

- **Histological types:**
  1. Minimal change nephrotic syndrome: MCNS "85% bet. Age gps 2-6yrs"
  2. focal segmental glomerulosclerosis: FSGS "10%"
  3. membranous proliferative glomerulonephritis MPGN "5%"

<u>IgM nephropathy:</u>
Same put it under MCNS & other put it separately b/c. is different in term of response to therapy. Beside it is MCNS except there is IgM deposition within mesangium of kidney.

Notes:

- Between the age of 2-6 or 8 yrs of life MCNS is the commonest it can reach up to 85% while FSGS 10 %, all other 5%. So other types are less common in pediatrics than in adult.
- Between age of 10-18yrs of life MCNS still the commonest but with less percentage drop 60%.
- No need for biopsy in every child with N.S. b/c. they can be treated invariably as MCNS until proven otherwise
- Indication for renal biopsy: these are the main indication for renal biopsy to look for histological type.
  1. Freq. relapse N.S.
  2. no response to treatment
  3. Steroid dependant N.S.
  4. Steroid resistance N.S.
- The main aim of renal biopsy is to differentiate b/t. MCNS and FSGS b/c. they are the commonest and FSGS has poor prognosis.
- 50%of FSGS pt. will progress to end stage renal failure in 5yrs; so, you have to identify them early, treat them and follow them.

- **Investigation:**

Ist line:

1. Urine analysis and pt. protein creatinine ratio
2. CBC
3. RFT: to know if there is some thing affecting the kidney
4. lipid profile : for confirmation of diagnosis
5. serum albumin

Others; 2nd line:

1. Complements "C_3- C_4": are usually normal b/c. MCNS is the commonest, if they are abnormal "low level" think for other causes and u may consider renal biopsy.
2. ANA: b/c. there are many c/t diseases that affect the kidney, this is for screening for that.
3. ANCA:
   - definitely is not a 1st line
   - is not needed until u have a reason
   - SLE don't give u +ve ANCA
   - SLE gives :
     +ve Anti dsDNA
     +ve antiphospholipid Ab
     +ve ANA
     ANCA: +ve in case of Wegener and poly arteritis nodosum PAN which is usually rare.
4. LFT: generally is not needed, but some time can be valid b/c. there is a certain type of N.S. like MPGN could be related to hepatitis
5. Renal biopsy: is not need as 1st line
6. US. : Really will not tell any thing a part from enlarge, echogenic kidney which is really not specific and not help toward the diagnosis.

- **Treatment of N.S.:**

1. supportive
2. definitive

Supportive:

Main aim is to take care of edema

Reasons of admission:

1. Generalized edema "anasarca" while simple edema e.g. puffy face in every morning does need for admission

2. Serum albumin <2 g/dl: which result in sever edema, so will not response to simple diuretic .so, we need infusion of albumin so, pt. has to be admitted.
   So serum albumin <2g/dl is an indication for albumin infusion to increase oncotic pressure to allow fluid to pass from extra vascular space to intravascular space then diuretic can be given but this type of treatment is temporarily.

What is the supportive Rx?

- If serum albumin >2g/dl ,give only diuretic
- If serum albumin<2g/dl +significant edema , albumin infusion if indicated in addition to diuretic
- S/E of albumin infusion :can lead to increase risk of volume over load and pulmonary edema

3. fluid and salt restriction
4. Any associated condition u have to care of it e.g. infection treated with antibiotic. However child with N.S. does not need Ab in general.

- **Definitive Rx.**

Steroid

Dose: current recommendation is to give "this is 1st episode" 60mg/m^2/d or 2mg/kg/d:

1. Daily for 6wks
2. Then alternating day" every other day" for 6wks
3. Then tapering the dose for another 2-3mon.

So total duration is about 6 Mon.

Until recently (i.e. in the past) 4wks daily and 4wks every other day was used instead of 6 wks daily and 6wks every other day.

Regarding the dose of steroid there were 2 studies:

1. hallmark study which is called international study of disease of child which is prove that 4wks,4wks is good enough in which the child is going for remission , do well and get very little s/e.
2. Another study which is proving that 6wks, 6wks has more S/E. than 4wks, 4wks.

So, they consider 4wks, 4wks as good enough but then tapered recently and replace by 6wks, 6wks why?

b/c. there is another study which is

3. German study of pediatric nephrology which again proves those 6wks is better and reduces no. of relapses but it has more S/E. than 4wks.

However, they found that pt. that is in 4wks Require more steroid b/c. of increased no. relapses so over all dose of steroid in 4wks Is more than 6wks, 6wks so the S/E. of the 4wks, will be more than 6wks.

Conclusion:

That is why the recommended dose knows every in 1st episode is in 6wks, with tapering of 2-3 Mon.

Note: over all pt. with N.S 2/3rd "60%" -3/4th "75%" or more will have a relapse. And only of 30%- 40% of pt. with N.S. will have only one episode without relapse.

- **Definitions:**
  - Relapse:
    - proteinuria appears earlier than edema so, for definition of relapse we use the term of proteinuria instead of edema " note nelson use term of edema in stead of proteinuria"
    - i.e. recurrence of proteinuria for 5-7 consecutive days without infection or stress
    - B/c. in case of stress or infection there will be increase protein in urine.
    - Proteinuria it has to be persistence 5-7d b/c. if not persistence (e.g. only last for 3 d. and then disappear, there will be no need for Rx. And this is what is called spontaneous resolution or remission.

  - Remission:

    I.e. disappearance of proteinuria in response to Rx. (Urine trace or +ve for 3 consecutive days, this is from nelson).

  - Freq. relapsing N.S.:

    I.e. recurrence of N.S. for >= twice/6mon or >= 4 times /12mon.

    It is an indication for renal biopsy.

  - Steroid resistance N.S.

    i.e. N.S. that not response in 6-8wks of steroid treatment, continues of proteinuria after 6-8 wks of therapy.

    If 4wks without response "suspicious", needs more follow up.

  - Steroid dependant N.S.:

    i.e. N.S. that is response to steroid Rx. When steroid is stopped or decrease during tapering, it will recurrence.

I.e. recurrence of proteinuria during Rx. Or within 15d of stopping.

Indication of renal biopsy:

1. Freq. relapse N.S.
2. no response to treatment
3. Steroid dependant N.S.
4. Steroid resistance N.S.
5. Others e.g. age <2yrsor >10 yrs, associated hypotension or renal dysfunction.

Continues definitive therapy:

Alternative drugs: whenever immature suppressive therapy are used renal biopsy are indicated.

a. cyclosporine
b. cyclophosphamide
c. chlorambucil

This only theoretically and pediatricians no use it

a. cyclosporine
3-6 mg/ kg/ day. Used for pt. with FSGS.

b. Cyclophosphamide + chlorambucil: both can be used even before renal biopsy, b/c it does not change.
So, if there is a pt. who is steroid dependant, frequent relapse, normal otherwise these medications can be used even before renal biopsy.
c. Chlorambucil: is very less frequently used.
d. Cyclophosphamide: is used for more common (2-3 mg/kg/day for 8-12wks). Is good drug but be aware of it is S/E (u have to follow up the pt. for S/E)
Main S/E is bone marrow suppression, lead to neutropenia (quickly develop) + hge cystitis, although the dose is very low in compare to that used for chemotherapy. So, u need to check WBC / wk initially for 3-4wks if its stay well, then u can stop checking or check it every other wk or less freq.
U have to use steroid daily or every other day, when he get remission tapering the dose.

- **Complication of N.S.:**
  1. Infection
  2. Thrombosis or hypercoagulability
  3. Iron def. anemia
  4. Hypothyroidism
  5. Complication of treatment.

1. <u>infection</u>
   d.t.:1. Loss of properidin which is cofactor that helps bacteria to attach to WBC for engulfment to opsonization
   2. d. t. fact that WBC of N.S, pt. don't move normally as other people.
   3. d. t. edema
   4. Loss of immunoglobulin
   5. Loss of complement.

   Most common infections are 1. Peritonitis 2. Cellulites
   Causative organism:
   Streptococcus "commonest", pneumococcus, H. influenzae, gram –ve, staph
   Rx. 2^{nd} or 3^{rd} generation cephalosporin+ cloxacillin or methicillin or may be vancomycin, depend on our area +type of resistance

2. <u>Thrombosis or hypercoagulability:</u>
   d.t. 1. Loss of antithrombin which is a fibrinolytic agent,
   2. Increase fibrinogen+ clotting factors: hepatic synthesis esp. vit K dependant clotting factor which are 2, 7, 8 and 9
   3. Decrease volume which leads to increase conc. "hyperviscosity.
   This lead to:
   a. Renal vein thrombosis: N.S. in relapse CCC. Red color urine, increase amount of volume and big mass in abdomen.
   b. Sagittal sinus thrombosis which is intractable.
   c. Intra arterial thrombosis: lead to intermitting claudication. D.t. involvement of leg vessels mostly.

3. <u>Iron def. anemia: d.t.</u>
   Loss of iron binding globulin which is a protein.

4. Hypothyroidism: d.t. loss of thyroid binding globulin.
   This is not a true hypothyroidism but the last shows "decrease TFT" which suggest hypothyroidism which later on end with significant

5. complication of treatment:
   Endocrine: Cushing syndrome, glucose intolerance, wt. gain moon face and buffalo hum
   GIT: peptic ulcer
   Musculoskeletal: growth retardation, osteoporosis, proximal myopathy.
   Eye: glaucoma, cataract
   Skin: striae, acne, hirsutism, skin atrophy.
   Hematology: poor wound healing
   CVS: HTN d.t. *up regulation of β receptors and salt, H2O* retention
   Increase risk of infection d.t. decrease of immunity.

Urinary tract infection (UTI)

- Definition:
  It is infection of the UT.

- Classification:
  Anatomical classification
  1. upper UTI: ‘ pyelonephritis’
  2. lower UTI: ‘ cystitis’ & ‘ urethritis’

  Usually we did not see urethritis.

  - Is UTI different in female (F) and male (M) children?
    Yes.
    Urethritis is more common in F because of the anatomic location. It is shorter in F and closer to the vagina and anus. So, it is easily expose to the secretions. Also, this is why ascending infection is more common in F than M.

  - Shall we treat them equally or with more concern to one?
    < 1 year of age UTI is far more common in M than F. but above this age and up to adulthood it is far more common in F than M. and this is also because of anatomical structures variations.

  - Under age of 5 we have to get more concern to UTI in both M & F Why?
    - Because normal child under the age of 5 still has small chance to get UTI; unless there is under lying abnormality. So, we have to get concern to the under lying abnormality.
    - There is separate abnormality for M & F:
      - the commonest under lying abnormality in M to develop UTI is Posterior Urethral Valve (PUV)
      - While in F is Vesicoureteric Reflux.
    - This is does not mean that other abnormalities are not possible.
    - Almost always PUV is not possible in F but Reflux is possible in M.
    - But bladder dysfunction in F is equal to PUV in M which either they can have neurogenic bladder or non neurogenic bladder or detrusor sphincter dyssynergia..etc. in these cases somehow bladder does not empty urine completely which prone to infections.

- How does upper UTI differentiated from Lower UTI in regard to clinical presentation?
  - Upper UTI usually presents with Fever, malaise, and flank pain. while Lower UTI presents with frequency, urgency, dysuria, …etc. but unfortunately these symptoms are difficult for 2 year old child to mention all what will s/he do is to cry. But above 5 or 6 is clear.
  - But upper UTI is systemic infection so they have fever, vomiting, lion pain but usually they do not have lower tract symptoms. Urethritis per say is not common in pediatrics. It is more in adult with STDs.

Cystitis:

Case scenario:

7 years old boy presents to you with history of lower abdominal pain, frequency, urgency, dysuria, with mild fever. So, you decided to do urine analysis and you find some abnormality and you decided that it is cystitis.

- What are the organisms that give cystitis?
  - Mostly viruses but bacteria can cause cystitis. All bacteria that give UTI can give cystitis.
  - Mostly E.coli because it has particular affinity to the transitional epithelium of the bladder. This affinity because of expression of vibrio antigen in the E.coli cell wall.

  - Most common viral cystitis is hemorrhagic cystitis which is caused by adenovirus. It is a self limited disease.
  - So, its treatment is supportive just drinking fluids and mild pain killer. It takes 72 hrs for acute symptoms to resolve.
  - Usually family comes frighten because of gross blood in the urine. But you see a lots of RBCs not much of WBCs. So, it is mainly clinical diagnosis.

  Because the definitive diagnosis is either:

  1. Urine culture for adenovirus and it will take long time.
  2. Serology: do IgM for adenovirus now and then do it after 4 wks.

  - So, basically patient will be fine by the time you find the diagnosis.

- Cystitis in older children usually comes with hematuria and a lot of local symptoms.
- Bacterial cystitis mostly by E.coli and Klebsiella. And treatment by antibiotics Bactrim (sulfamethoxazole and trimethoprim)

- **Upper UTI ' Pyelonephritis'**

Case scenario:

3 years old boy comes with history of high grade fever, lethargic, vomiting and he makes his mother change his diaper more often because he made it wet; with bad urine smell.

- ***What questions to be asked in history?***

- Is he febrile?
  - Yes, he has fever of 39^{o}C for 2 days.
- Does he have loin pain?
  - He is child, but he cry when you touch his loin.
- Are these symptoms is the first time or does he has similar symptoms before?
  - This is the most important question.
- Does he circumcise?
  - Although in our part of the world 99.99% of boys are circumcised but it is a valid question.

- On Examination:
  - Look for signs of dehydration.
  - BP measurement is the most important measure in pyelonephritis. Because pyelonephritis is associated with high BP.
  - Local examination (abdomen)
  - Any masses ' he may have cystic kidney, duplication, multicystic dysplastic kidney …etc' . Even a distended bladder.
  - It is also important to take weight and height to differentiate between Acute and chronic.

- Investigation:
  - Urine Analysis.
  - CBC
  - RFT

- Urine and blood culture and sensitivity
- RUS
- Voiding Cystourethrogram VCUG.
- DMSA Scanning.

► Urine Analysis:
Look for gross appearance, color, small volume,..etc which are not specific for UTI.
The 3 most important things in UA are:

1. Presence of WBCs
2. Leukocyte Esterase
3. Nitrates

- If these 3 present you can be sure that patient have UTI in 90% of cases. If two are present the sensitivity drops to 60%.
- Other important thing is WBC cast. While RBC cast is not helpful in UTI ‘ It is present in GN’ .

► ***Urine culture:***
The methods of urine sample collections are:

1. Catheterization
2. Suprapubic Aspiration
3. Mid stream clean catch.
4. Bag

➲ Bag:
Useless because of contamination with skin or stool but there are few special circumstances:

- Young patient in whom your index of suspicion is low and you are not going to give him antibiotics. So, it is just a screening test. But if it is come positive, then you will get an appropriate sample and culture either by cath or Suprapubic Aspiration and start treatment. So, bag specimen is only done for screening but you do not treat according to its result.

➲ A midstream clean-catch (MSCC):

- Done in children who are toilet train. Usually about 5 years old.

➲ Suprapubic Aspiration (SPA):

- You can not do it after 2 years of age because bladder becomes a pelvic organ. 2 finger width above the

symphysis pubis in the mid line. Then, go perpendicularly in to avoid injury of near by viscera. That is why after the age of 2 you do not do SPA.

► ***CBC and Blood culture:***
You will look for high WBCs or anemia in chronic cases. Blood culture needed because in pyelonephritis 30 – 40% will have positive culture.

➲ Interpretation of Yield of culture:
- Bag:
  Positive urine culture by a bag specimen is 100,000 colonies/100ml of any single organism.
- MSCC:
  100,000 colonies/100ml of single organism
- Catheterization:
  1000 colonies/100ml
- SPA:
  Any colony even single one of any organism.

► Common organisms causes pyelonephritis:
E.coli, Staph, and enterococci.
Instrumented or immunocompromised patient may get pseudomonas, candida, and staph.

Culture result required 24-48 hrs.
So, any child with pyelonephritis needs admission for receiving IV treatment.

➢ ***Treatment***:
- Started empirical IV antibiotics:
  - Ampicillin " mainly G +ve" + Gentamicin " mainly G- ve" . Ampicillin gives synergistic effect to gentamicin. But Dr does not prefer this protocol because gentamicin is nephrotoxic. or
  - Cefotaxime or
  - Cefuroxime.
- Maintain IV fluid.
  Until culture result reaches then look for sensitivity result and stick with it.
- Then in 48 hrs you should repeat urine culture to ensure that urine is sterile.

- Then, you should evaluate urinary tract by RUS and VCUG.
  We have two types of VCUG:
  1. Conventional ' this is should be done first' .
  2. Nuclear ' less radiation but it has limitation that it does not delving the lower UT (urethra). So, first time VCUG should always be conventional and the following you can do nuclear. Depending on result you will decide what to do.

  - Timing of VCUG: "ideally" should be done when negative culture is there.
  - " previously" people tends to do VCGU 4-6 wks although it is valid but there was a problem of patient lost follow up. So, that is why the new recommendation to do VCUG as soon as negative culture there.

- How long to treat?
  10-14 days. 5-7 days IV and rest can be PO

Reflux grades:

I. Reflux at lower 1/3 of ureter
II. Up to pelvis
III. With dilatation
IV. With calyces ballooning
V. With tortuous ureter

Up to grade 3 just prophylactic antibiotics + 1-2 time/ year VCUG.
Grade 4 and 5 consult urologist.

► ***Follow up:***

Surveillance for recurrence ' Dr does not recommend it because of false positive result' , but the recommendation is to do VCUG after 1m, 3m, 6m and then every one year.

Then, I tell the family that once child get fever of concern try to consult the pediatrics nephrologist clinic.

5-6 months after pyelonephritis do DMSA scan to look for presence of kidney scaring (functional). Basically any child get UTI need follow up for 1 year.

Hypertension

- **Definition:**

Increase in systolic and\or diastolic BP above the 95th percentile for age, gender and height.

- **Report about BP in pediatrics**

In 1977 at which they recognize that hypertension can happen in child.
1986 gives the oldest norm of BP.
1996 comes with an idea that BP is not just related to gender but also related to the height.

It is found that taller children have higher normal BP than shorter one. So, start thinking that height can make differences.

Aug. 2004 gives more divisions about hypertension which are 50th, 90th, 95th, and 99th percentile which make change in the general definition previously mentioned to fact that the hypertension can be divided in two stages:

- Stage 1 HTN

Any child whose BP is 95th percentile + 5 mmHg. Here there is a time to look for the cause before ttt can be started.

- Stage 2 HTN

Any child whose BP is 99th percentile + >5 mmHg which is actually an acute emergency. It has to be treated before you look for the cause.

- Stages of hypertension

1- Normal	<90th percentile for 5 +\or D
2- prehypertensive	90th -95th percentile or 120\80 mmHg
3- Actual HTN	>95th -99th percentile
4- Accelerating HTN	≥99th percentile

- **Method of measuring BP in pediatrics**
  - Sphygmomanometer
  - Mercury (manual)
  - dynamic (automated or oscillometry)
  - Aneroid

1- mercury: is toxic and it has a lot of variable that can be affected which are:

Depends on how your ears are? And which sound you take (K4 or K5)?
That is why mercury is not used any more and automated or dynamic are usually use for measuring BP.

2- dynamic: easer, measuring only systolic BP while diastolic BP is actually calculated BP so is not true DBP and the BP getting by this method is not accurate but that is what we have.

- **Size of the cuff**

For appropriate size of cuff:

- The cuff width of the bladder should cover 2\3 of the length of the upper arm.
- Circumference between 40%-80%

Size of the cuff is very important because bigger cuff under estimate BP whereas smaller cuff is over estimating BP

- **In BP assessment is very important:**

1- To take an appropriate size of cuff
2- To know method you are using
3- To know the height and gender
4- Go to chart and find if BP is normal or not

- **Requirement for taken correct BP:**

1-Patient has to be rested for at least 5 min in clinic or nurse office before BP is taking
2- You need to repeating reading before decide either BP is normal or not. This repeating reading has to be 3 in times and simultaneously because more time in taken BP, more rise in BP so better to take BP in once brief sitting position than separating reading

But the patient who comes to you with too high BP e.g. (200\130) you have to treat immediately. But those in border line you have to wait. Because it is not an emergency so you can call them later

So both the norms and the method of taking BP are very important for correct measuring BP

BP should be taken from the arm (usually right arm) at the level of the heart in sitting position (better)

Normal LL pressure is higher than UL pressure

Recommendation for taking BP

All child above the age of 3 years unless there an absolute reason for taken BP in those who are less than 3 years of age such as:

- Premature infant
- Heart disease
- Renal disease
- Congenital anomalies

So in normal child up to 3 year of life no need for taken BP but those more than 3 years you should take BP

How to know that this BP is normal or high:

For child under the age of 2 years you have to blot the reading in the chart (normogram)

For child above 2 years of age it can be estimated by the following:

SBP----------100 + (2.5 × age)

DBP---------- 70 + (1.5 × age)

e.g. for child with 10 years of age normal BP is 125\95 mmHg

Etiology of HTN

1- Essential is rare in pediatric age group

2- 2ry HTN 70%-80% (is the commonest)

- Renal (is the commonest)
- CNS
- Endocrine
- CVS
- Drugs

1- *Renal causes (most common)*

a) Renal parenchymal disease (is the most common among all renal causes)

60-70% of all renal HTN

GN, renal failure, renal transplant (more common), cystic renal disease, dysplastic kidney, polynephritis, renal tumor (Wilms tumor and neuroblastoma)

b) Renovascular disease

- Renal artery stenosis
- Hemolytic uremic syndrome
- Polyarteritis nodosa
- Lupus

2- Endocrine

- Thyrotoxicosis
- Pheochromocytoma due to hypercalcemia which lead to increase vascular tone and increase PVR then to HTN
- Hyperparathyroidism
- Cushing syndrome due to defect in Na\Cl channel
- Conn' s syndrome
- Congenital adrenal hyperplasia

3- CNS causes

- Any thing cause increase ICP
  - space occupying lesion
  - pseudo tumor cerebri
  - abscess
  - infection
- Seizure
- Gillian-Barré syndrome

4- CVS causes

Coarctation of the aorta is the commonest

5- Drug

Steroid

Cyclosporine vasoconstrictor ------increase PVR then to HTN

Amphetamine

Diagnosis of HTN

- From history:
  - Change of urine output, urine color, body fluid status, growth status for renal pathology
  - Change in perfusion in upper or lower limbs for coarctation of aorta

- Joint pain, oral ulcer, skin rashes for connective tissue disease
- Increase or decrease appetite, weight, tachycardia, intolerance to hot or cold for thyroid disorder
- Polyuria can be found in case of hypercalcemia

Adenoma sebaceum--------- neurocutaneous syndrome (neurofibromatosis + tubular necrosis) both are usually associated with renal artery stenosis

- From physical examination:
  1- Volume of pulses
  2- Four extremities BP is very important in case of coarctation of the aorta
  Normally LL > UL BP but in coarctation of aorta LL < UL because blood can't reach the lower limb easily

Investigation

In general investigation can be divided into 3 line or stages

- **Stage 1:**
  - CBC
  - RFT
  - Ca (for hypercalcemia)
  - Phosphorus
  - Lipid profile for metabolic acidosis
  - ECG + Echo cardiogram for effect of HTN on heart
  - Renal US
  - Uric acid (because child with high uric acid more likely to have essential HTN)
  - Electrolyte
  - Blood sugar
  - Urine analysis and urine culture (for pyelonephritis)

- **Stage 2 for looking for specific causes:**
  - US
  - Voiding cystourethrogram→ look for vesicoureteric reflux
  - Captopril renal scan→ indirect way to diagnose RAS
  - 24 hrs VMA and catecholamine→ for pheochromocytoma

- **Stage 3:**
  - Renal arteriogram
  - Renal vein renin level (RAS)

  It should be done from RT and LT side. The side with RAS will show higher level of renin

Management of hypertension

- HTN emergency
- Any child with hypertension

- **HTN emergency**
  - These patients who come with symptom of hypertension
  - These patients need some method of treatment which is fast and titratable (can ↑ *or* ↓ *effect of medicine* quickly)
  - These patients should be in ICU setting to monitor by intra arterial BP measuring device and give him continuous drug therapy that can be given as continuous infusion and can be monitor (titratable)

1- Na nitroprusside
2- Ca channel blocker (Nicardipine)
3- *Labetalol (α + β blocker)*

2 and 3 are safer than nitroprusside because of no cyanotic toxicity

<u>Na nitroprusside:</u>
Cyanotic toxicity
Photo labile (we need to cover it by albumin) because if it exposed to light it will not work

- **Aim of ttt of hypertension emergency**

  Is to reduce BP by 25 % in first 6-8 hrs and then bring it to normal over the next 2-3 days

Don' t reduce BP rapidly (within few hours) because it decrease perfusion pressure and lead to brain and renal ischemia

- **Antihypertensive classes**
  - Diuretics
  - Sympatholytic
  - Vasodilator
  - ACEI
  - ARB most newest drugs
  - CCB
  - Centrally acting
  - Ganglion blocker

➲ ***Diuretics***

- Thiazides considered as a drug of choice for essential HTN in adult
- Furosemide (lasix) it is usually for short term because of side effects:
  - Hyper calcinosis lead to nephrocalcinosis (main S\E)
  - Hypokalemia(rare)
- That is why lasix is not use for long term
- Any overload problem can be treated with lasix

➲ ***Ca channel blocker***

- Nifedipine---------- short acting
- Amlodipine---------- long acting (once daily)

➲ ***Beta-blockers***

- Propranolol---------- which is not specific

➲ ***Alpha and beta blockers***

- Labetalol---------available in oral form and can be used for long term

➲ ***ACEI***

- is a drug of choice once bilateral RAS is excluded (can be used in unilateral RAS)
- captopril (short acting 4times\day)
- enalapril (long acting 2 times\day)
- lisinopril (long acting 1 time\day)

➲ ***ARB***

- most recent drug and mostly used in adult
- can be combined with ACEI for better effect

➲ ***centrally acting***

- methyl dopa: seldom to be used only in pregnancy
- clonidine: has many dosage form (oral, cutaneous patch (once per wk so high compliance)

➲ ***vasodilator***

- hydralazine (safest) s\e is lupus like
- diazoxide s\e hyperglycemia + hypertrichosis
- minoxidil s\e hypertrichosis

⅄ **choice of drug depend on the cause of hypertension**

e.g.

➢ **GN** → start with diuretics then CCB and when patient is stable we can use ACEI

➢ **Bilateral renal artery stenosis** → CCB + labetalol (don' t use ACEI)

➢ **Essential HTN** → ACEI in pediatrics

➢ **Transplantation** → mostly related to steroid and cyclosporine so we use either diuretics for short time or CCB for long time. In case of cyclosporine CCB should be use simultaneously to counteract s\e of cyclosporine

➢ **Pheochromocytoma**
We use alpha and beta blocker
Labetalol or propranolol + ventolamine(or prazocine)

Regarding the dose of drug the doctor said is not important

Acute renal failure

- **Functions of kidney**

  1-excretion of waste products e.g. urea, ammonia
  2-secretion of hormones
  3-sodium and water homeostasis
  4-acid base balance

So, renal failure is not a cessation of one of them. It is whenever the whole body homeostasis is affected.

- **Renal failure is classified as:**

  A- oliguric: urine production is less than 1 ml/kg/hr ($400ml/m^2/day$)

  B- non-oliguric

- **Notes:**
  - Anuria has to be for 24 hrs, but when pt is oliguric we suspect anuria and don' t wait.
  - Most of cases in pediatric are reversible.

- **Definition of ARF:**
  - Rapidly progressive cessation of renal function
  - Inability to maintain body homeostasis
  - Retention of nitrogenous wastes
  - Fluid and electrolyte imbalance
  - Often decrease urine output
  - Usually reversible

- **Etiology of ARF:**
  - pre-renal
  - intrinsic renal :
    - -acute GN
    - -interstitial nephritis
    - -vasculitis
    - -acute tubular necrosis
  - post-renal

Pre-renal and post-renal causes are functional disorders. That means at the beginning there is no structural change in the kidney histology. For example in post-renal there will be back pressure that leading to histological change later on. Similarly in pre-renal the primary event is dehydration or mal-distribution of the volume (volume overload but not in the intravascular components and it has to be intravascular to be Sensed). You should rule out pre and

post renal causes first because they may lead to acute tubular necrosis.

- **Pre-renal etiology :**

  1-decrease effective circulatory volume

  A- hypovolemia: GI losses, hemorrhage, renal losses, cutaneous losses

  B- distributive: may be there is excessive fluid but with mal-distribution, third space losses, hypoalbuminemia, shock, sepsis, antihypertensive medication, bilateral renal artery stenosis/ thrombosis.

  2- Decrease cardiac output

- **Intrinsic renal etiology :**

  1-acute tubular necrosis:

  - Ischemia
  - Nephrotoxin: exogenous, endogenous
    - e.g. exogenous like drugs:
      -antibiotics: aminoglycoside
      -antifungal: amphotericin B
      -antineoplastic: bleomycin causes retroperitoneal fibrosis → obstructive uropathy.
    - Endogenous:
      Hemoglobin (hemolysis),
      myoglobin(rhabdomyolysis)

  2- Interstitial nephritis:

  - drugs induced :sulfa drugs ,furosemide "LASIX", erythromycin, penicillin
  - infection :sterpt, infectious mononucleosis
  - infiltrative lesion "tumor" : rare in pedia

- **Post-renal etiology :**
  - Congenital abnormalities:
    - Post. Urethral valves: always in males
    - Neurogenic bladder: mostly in females
  - nephrolithiasis: must be in the urethra or staghorn calculi
  - drugs: Anticholinergic cause urinary retention
  - traumatic injury
  - Tumor

Pathophysiology of acute renal failure:

TUBULAR CELLULAR INJURY :

- change in cellular metabolism
  - fall in cellular ATP
  - reactive oxygen molecule
  - increased intracellular Ca
  - phospholipase breakdown of membrane
  - loss of cellular polarity
- intratubular obstruction
- back leak of glomerular filtrate

VASCULAR FACTORS :

- impaired autoregulation
- vasoconstriction
  - Increased rennin –angiotensin
  - ? prostaglandin inhibition
  - Increased endothelin
- Reversal of vascular factors does not result in amelioration of ARF.

Diagnostic approach :

80% can be diagnosed by Hx and exam.

History:

Anuresis	dripping
Dysuria	burning sensation
UTI symptoms	trauma
Liver problems	heart disease

- Recent URTI: post infection nephritis
- Volume loss: Vomiting, diarrhea [gastroenteritis]
- Congenital anomalies
- Hx of recent drugs ingestion
- Hx of skin rash and joint pain
- Hx of bloody diarrhea, vomiting, red urine, red spots all over the body: hemolytic uremic Syndrome
- Family Hx of ARF: hereditary nephritis ON/OFF hematuria
- Hx of repeated sinusitis /repeated pulmonary bleeding →Wegener granulomatosis
- Hx of recurrent gross hematuria from URTI, HTN proteinuria →IgA nephropathy

- **Physical examination:**
  - To determine how bad is RF
  - Give a clue toward diagnosis
  - Ascertain the cause
  - The important points of examination are:
    Edema – signs of dehydration – BP-murmurs- using of glasses- hearing loss or not – skin rashes

- **Lab. Evaluation:**
  - CBC with peripheral smear " general evaluation"
    Hb helps in determine if acute (normal level) or chronic (never normal)

  - Electrolyte, BUN, creatinine
    These are definitely indicated because they might tell you what problems the patient has and if acute or chronic

  - Ca, PO_3, ALBUMIN:
    High Ca, low PO_3 → mostly chronic
    Albumin helps in assessment of general health, nutrition, and proteinuria

  - Urine analysis: it is the medical biopsy of kidney, look for (specific gravity, cellular elements, and casts) ex. RBCs casts in urine Indicate GN

  - Urine electrolyte should be done prior to giving either fluids or diuretic because once the patient take diuretic, urine electrolyte content will change remarkably and become unpredictable.

  - Urine indices:

	Prerenal	**renal**
Na urinary	**<20**	**>20**
BUN/Cr	**>20**	**<20**
FENa	**<1**	**>1**
Urine Osmol.	**>500**	**<350**

Comments:

1- Plane urinary Na not helpful because it is directly affected by salt ingested with food.

2- FENa is used to measure tubular function and it is helpful more than urinary sodium. In neonates up to 2.5 is normal because of immaturity of kidney, they attain normal adult level of function by 2years of age

$$FENa = \frac{(\text{Urine Na} / \text{P Na})}{(\text{Urine Cr} / \text{P Cr})} \times 100$$

3- Regarding BUN/Cr ratio, there is a problem because this is a division factor and any change in one or other without changing function will affect ratio, e.g. anybody who is on steroids will be in catabolic state and therefore elevated BUN. so , the ratio will go high and gives false picture that indicate dehydration while it might be not true . Similarly if the patient has gut bleeding will have high BUN "degradation of Hb" on contrary somebody who is thin and emaciated will have low level of Cr and looks like dehydrated.

4- The important thing to know that these measures are valid before the management

- Radiological studies " torule out obstruction "
- Additional lab. Work up
  Wegener's → ANCA
  Lupus → anti-dsDNA, antiphospholipid
  Goodpasture → antibasement membrane antibodies
  Post strept. → ASO titer, C3 and C4 level, Antihyaluronidase
- Percutaneous renal biopsy:
  Usually renal failure recovers minimum within 7-10 days and maximum within 4 weeks. If function has not returned at least to some degree in 4 weeks that means it will not return so take biopsy to ascertain the cause.
  So, renal biopsy is not essential to diagnose renal failure.

- **Metabolic problems :**
  - Hyperkalemia
  - HTN
  - Fluid overload
  - Hypo/hypernatremia
  - Acidosis
  - Anemia
  - Hypocalcemia
  - Hyperphosphatemia
  - Neurological symptoms d.t BUN or middle molecules

- **Management :**
- **Preventive:**
  - All acute renal failure patients are considered dehydration or prerenal failure until proven otherwise.
  - First give volume bolus 10-20ml/kg NS (1-3 bolus depend on patient status and clinical judgment)
  - Next if no urine output give diuretic “furosemide” (1-5 mg/kg IV)
    - **Effects:**
      - Strong
      - Increase intratubular flow
      - Renal vasodilation
    - **Side effects :**
      - Hypokalemia
      - Hypovolemia
      - Ototoxicity

- **Supportive:**
  - Fluid restriction:
    - After the patient urinate, start usual maintenance and dehydration protocol but if not fluid restriction is applied.
      Net insensible water loss (NIWL) + measured losses
      NIWL = 400 ml/m^2/day
    - Increases with fever, burns, tachypnea

  - Measured water losses: urine output, GIT losses, others

Management of special potential problems :

Hyperkalemia :

- It is very important because kill fast
- How to determine if emergency:
  1- k > 7.5 m eq/l
  2- ECG changes:
  Peaked T waves
  Prolonged QRS
  Ventricular arrhythmia
- Treatment:

SHORT TERM:

Ca gluconate / $NaHCO_3$ /glucose and insulin /β-agonist

The effect will not change potassium level but redistribute it

LONG TERM:

Kayexalate/dialysis

The effect will get rids of potassium

Drug	Action
Ca gluconate (10%) ml/kg over 10-15 min	Acts immediately but lasts only for minutes, it stabilizes membrane
$NaHCO_3$ 1-2 mEq/kg IV over 15-30 min	Onset 30 min , lasts 1-2 hours; shifts K intracellularly
Glucose 0.5-1.0 gm/kg with Insulin 0.1u/kg over 30-60 min	Onset 30 min , lasts 1-2 hours; shifts K intracellularly
Albuterol nebulization ml/kg/dose	Onset 30 min , lasts 1-2 hours;
Kayexalate 1gm/kg PO/PR (through NG tube is better) per rectal cause osmotic diarrhea	Onset in hours , lasts for hours

- **Acidosis :**
  - Anion gap acidosis due to retention of organic and inorganic acids
  - Avoid NaHCO3 if patient is hypernatremic or severely fluid overload.

  - The patient must have normal serum and prior to giving because it will reduce ionized and shift to cells. Even if is normal you have to be careful because hypokalemia itself may cause concentrating inability, myopathy.

- Base deficit = $0.6 \times \text{wt} \times (HCO_3 \text{ desired} - HCO_3 \text{ observed})$ / 2

- **Hypocalcemia**
  - due to phosphate retention
  - vit.D deficiency & PTH resistance
  - due to foods containing phosphorus
  - RX with Ca carbonate "binds phosphate in the gut" and you can give vit.D analogues if Ca carbonate doesn' t help.

- **Hyperphosphatemia**
  - Phosphorus cannot be excreted because of failed kidney, so give phosphorus binders.
  - Phosphorus binders :
    1- Aluminum hydroxide: not used, it cause dementia and bone toxicity
    2-calcium containing phosphorus binders: cause deposition of Ca in heart and blood vessels.
    3-non Ca- non AL phosphorus binders: [lanthanum carbonate, sevelamer hydrochloride]
  - do dialysis if the level >15mg/dl

- **NUTRITION :**
  - No specific treatment for RF, so we support pt by adequate nutrition. If he pass urine this is good if not DIALYSIS. Limited proteins intake 1mg/kg/day.
  - No contraindication to use lipids.

➢ RENAL REPLACEMENT THERAPY :

➲ *Peritoneal dialysis:*

- efficient in infants and young child
- manual or automated cyclers
- limitation has to be done over at least 12 hr/day

➲ *Hemodialysis:*

- Pediatric/neonatal dialyzer, catheters and blood lines available
- limitation :
  -4-5hrs/day
  -need large pore vascular access
  -very tedious
  -it changes water and electrolyte balance quickly which can cause neurological imbalance known as DIALYSIS DYSEQUILIBRIUM SYNDROME.
  -through subclavian, external jugular or femoral vein

➲ *CAVH/CVVH "continuous veno-venous hemofiltration"*

- Ideal modality
- continuous therapy for slow fluid removal
- 30-50 or 20-30 ml/hr
- may remove immunomodulation substance in sepsis

➲ *Indication for renal replacement therapy*

1- Hyperkalemia with oliguria
2- Hyperphosphatemia >15mg/dl
3- Fluid overload, CHF, pulmonary edema
4- Intractable acidosis
5- Hyperammonemia
6- Dialyzable toxin e.g. amitriptyline
7- Inadequate nutrition "relative indication"
8- Uremic symptoms" bleeding tendency, seizure, sever itching"

Notes:

- BUN levels itself is not an indication unless associated with uremic symptoms
- itching is the least indication for dialysis

Diarrheal disorder

Definition of diarrhea:
Diarrhea is loose, watery, and frequent stool.

I-Aetiology:

A-Viral:

- Rotavirus
- Coxaci virus
- Echo virus
- Asco virus

(Coxaci virus, Echo virus) } Enteric virus

B-bacterial:

- E coli types:
- Shigella
- Salmonella
- V. cholera (cause epidemics)
- Staphylococcus aureus
- Campylobacter
- Yersinia *enterocolitica*

C-Parasite:

- Giardiasis *Giardia intestinalis (also known as Giardia lamblia)*
- Entamoeba histolytica
- Cryptosporidium in immunodeficiency

II-Pathogenesis:

1-Secretory diarrhea:

Watery diarrhea contains solutes (electrolyte)
Which will not stop by fasting so has great risk of dehydration.
Ex: V. cholera

2-Osmotic diarrhea

Mal absorption of solute (not electrolyte) so the osmolality more than electrolytes.
Does stop by fasting because of decrease in the osmolality caused by mal-absorption
Ex: lactose, laxative like lactulose

3- Decrease surface area

Short bowel (gut) syndrome which seen commonly in nursery babies who had intestinal resection.

4- Intestinal mucosal invasion
   Most infections cause invasion diarrhea
   Ex: sheigella
   Intero invasive E coli
5- Increase motility: as in irritable bowel syndrome (IBS)
6- Decrease motility: in blind loop syndrome lead to stagnation and bacterial growth

III-clinical presentation and diagnosis:

Dehydration is the most important and most dangerous condition
It is divided into three types: mild, moderate and severe.

- The mild one present by dry mucous membranes
- While the moderate by the following
  1- sunken eyes
  2- absent tears
  3- poor skin turgor
  4- depressed anterior fontanel
  5- delayed capillary filling
  6- thirsty
  7- dry tongue
  8- decrease urine output
  9- tachycardia
  10- Kussmaul breathing (rapid and deep)
- Severe type present by hypotension and shock

Determination whether caused by bacterial or viral agent

Variable	Bacterial inf.	Viral inf.
Fever	High grade >38.5	Low grade
Vomiting	More frequent	Less
Dysentery*	Present	Absent
ESR	High	-
CBC	bandemia	

*dysentery mean tenesmus with frequent passage of blood and mucous in stool

IV-investigation

CBC – bandemia of leukocytosis in case of bacterial infection
Stool smear –microscopic examination for parasite (E. histolytica)
Stool culture
Blood culture- in immunocompromised
RFT – serum electrolyte for dehydration specially Na which determine type of dehydration if it
   Iso
   Hyponatremia <130
   Hypernatremia >150

V- Management

a) Rehydration:

1-ORS (oral rehydration salt):

Of the WHO (http://www.who.int/medicines/publications/pharmacopoeia/OralRehySalts.pdf)

Contain glucose, Na, K and Cl

Can reduce diarrhea duration:

Because with each Attack of gastro-enteritis a process of degeneration to enterocytes take place, and it has been found that ORS promotes the regeneration of these cells. However patient on prolong NPO have longer duration of diarrhea because of enzyme deficiency which called 2ry lactose deficiency

Contraindication

- severe dehydration (hypotension, shock)
- comatose, LOC
- recurrent vomiting (must be recurrent and don' t use antiemetic)

2- Parenteral rehydration:

- Boluses 20cc given very fast, but if the dehydration is not that severe we can give it over 30-60 min
- Never ever forget ongoing losses (may lead to failure of treatment)
- How to rehydrate?

  Maintenance therapy

  1st 10 Kg – 1 Kg X 100cc = 1000cc

  2nd 10Kg – 1Kg X 50cc = 500cc

  Rest Kg – 1Kg X 20cc = depends

b) Antibiotics: (only bacterial diarrhea)

Amoxicillin

Trimethoprim sulfamethoxazole

Deficit therapy

Age	Mild	Moderate	Severe
<3 years	5%	5-10%	10-15%
>3 years	3%	3-6%	6-9%

Complications:

Hemolytic uremic syndrome

Shock due to renal failure caused by acute tubular necrosis

Immune deficiency syndrome

► Introduction:

- Immune system component:
  The major components of the immune system are:
  B-lymphocytes
  T-lymphocytes
  Phagocytes
  Complement

- There are Immune system side effects for example:
  Hypersensitivity
  Graft rejections

I- B lymphocytes:

Function:

Synthesis of major classes of antibodies (AB): IgA, IgM, IgG, IgE, IgD

1- Which protects against
Pneumococcus
Hemophilus
Staphylococcus
E. coli
Salmonella

2- Covering mucous membranes to prevent the entry of viruses and the establishment of infection.

Deficiency of B lymphocytes:

Recurrent proven of bacterial sepsis or meningitis by the previous organisms.

Note: recurrent and proven (because it cost a lot to investigate for immune deficiency)

II- T lymphocytes:

Function:

It is responsible for cellular immunity.

Types:
T helper, T suppressor, T killer.

T killer:
Kill viruses, mycobacteria, and parasite.

Containment of viruses before establishment of infection.
Containment of mycobacteria before establishment of infection.
Containment of parasite before establishment of infection.

Deficiency of T lymphocytes:

a- Recurrent viral infection:

So if we give life attenuated vaccines it will result in severe infection or inflammatory reaction.

e.g. measles vaccine → *measles pneumonia*
Varicella vaccine → *varicella pneumonia*
BCG vaccine → *disseminated infection.*

b- Recurrent oral and systemic candidiasis, mycobacterial infection:

It should be after 6 month of life to be significant because we might see candidiasis in normal neonates.

Investigation:

B lymphocytes:

1- CBC

Lymphopenia (not always)
Abnormal size

2- Immunoglobulin level:

Should be done after 6 month of age because of maternal Ig that pass through the placenta (IgG) but if the disease suspected is affected manly B cell do IgM level because this type can't pass through the placenta.

T lymphocytes:

1- Chest X-ray:

To evaluate thymus shadow.

2- Tuberculin test:

Which should be +ve for recent BCG recipients.

3- Quantitative measure for T cell subtypes:

CD4, CD8

Immune system disorders

B lymphocytes:

1- AGAMMAGLOBULINEMIA:

No immunoglobulin
Most severe form X-LINKED (XLA OR BRUTON) AGAMMAGLOBULINEMIA

Clinical:

- Recurrent proven of bacterial sepsis or meningitis after 6 month of age by:
  - Pneumococcus
  - Hemophilus
  - Staphylococcus
  - E. coli
  - Salmonella
- Otitis media
- Skin rash
- No enlarged lymph nodes even the tonsils.

Dx:

Ig level

Treatment

Administration of human immunoglobulin
Prophylactic antibiotic in case of infection or febrile illness.

2- COMMON VARIABLE IMMUNODEFICIENCY

Have some Ig
Delayed presentation in compare to previous
Not so severe

But still:

Having bacterial infection
Diarrhea
Skin rash

Dx:

Ig level

Rx:

Human Immunoglobulin

3- SELECTIVE IgA DEFICIENCY

The main antibody that covers mucous membranes, intestinal mucosa.

Clinical:

Most of the cases are asymptomatic and discovered during routine investigation

Upper respiratory tract infection and intestinal infection

Caused by: parasite, protozoa, and giardiasis.

Dx:

Ig level

Rx:

Human Immunoglobulin

4- SELECTIVE IgG DEFICIENCY

There are 4 subclasses of IgG:

2, 4 are mainly responsible for Polysaccharide antigens which present in encapsulated organisms (pneumococcal, hemophilus)

Dx:

Ig level

Rx:

Human Immunoglobulin

5,6- SELECTIVE IgM, IgE DEFICIENCY

Recurrent proven of bacterial sepsis or meningitis after 6 month of age.

Dx:

Ig level

Rx:

Human Immunoglobulin

- **T lymphocytes:**

1- THYMIC HYPOPLASIA (Digeorge Syndrome):

Embryology:

3^{rd} and 4^{th} pharyngeal pouches which give:

1) Parathyroid → *hypocalcemia → tetany*
2) Thymus → *hypoplasia → T cell deficiency.*
3) Part of the face → *low set ears, high arch palate*
4) Heart → *conotruncal structures*

Clinical:

- Mostly hypocalcemia and tetany.
- Abnormal facialis (low set ears, high arch palate)
- Cardiac: truncus arteriosus
  Aortic arch defect
  Teratology of Fallot
  Right sided aortic arch
- Immune system deficiency

Investigation:

- Chest X-ray for thymus shadow
- Serum Ca decreased
- Echo for cardiac defects.

Treatment:

Bone marrow transplantation.

2- Meslow syndrome:

They have thymic hypoplasia but no parathyroid or cardiac problems.

3- Cartilage hair hypoplasia:

- T cell deficiency
- Short stature
- Alopecia
- Neutropenia

Rx: BMT

Primary Combined Antibody and Cellular Immunodeficiencies

1- Severe Combined Immunodeficiency (SCID)

They have manifestation of both B &T cell deficiency in addition to:

a) Wasting
b) Failure to thrive.
c) Diarrhea may present

They usually die within 2 years of life.

Treatment: BMT

2- Wiskott-Aldrich syndrome:

- Combined Immunodeficiency
- X-lined recessive (mostly males)
- Thrombocytopenia
- Small size platelets
- Otitis media (draining ears)
- Intractable eczema
- Splenomegaly

Investigation:

High IgA and High IgE
But low IgM

3- Ataxia-telangiectasia:

- Cerebellar ataxia
- Telangiectasia in ears, sclera, and face
- Immunodeficiency
- Endocrinopathies: hypo-, hyperparathyroidism.

Investigation;

Low IgA, IgE, IgM

Treatment: BMT

4- Chronic mucocutaneous candidiasis:

Chronic recurrent candida of tongue, face, systemic candidiasis in addition to:

Poly-endocrinopathies (hypothyroidism, hypoparathyroidism)
Onychomycosis.

Complements disorders

11 components participate in immune response.

- Early component (C3, C4)
  Associated autoimmune diseases (SLE, rheumatoid arthritis, GN)
- Late components associated with:
  Recurrent Neisserial infection (gonorrhea, meningitidis)

Neutrophils

Protect against pyodermal infections: Piles, furunculosis (deep, superficial)

There are two types of deficiency

1- Quantitative deficiency:

Neutropenia

Associated with immunodeficiency like cartilage-hair syndrome and infection like salmonella.

Transient neutropenia:

The most common cause of neutropenia in otherwise normal child is viral infection.

2- Qualitative deficiency

Normal quality includes:

a- chemotaxis
b- Phagocytosis
c- Release mediator for intracellular killing.

Neutrophils disorders:

1- Chronic granulomatous disease:

When the defect in the intracellular killing

Clinical:

Suppurative LAP
Recurrent abscesses boils, furuncle, liver abscess.
Recurrent osteomyelitis.

Investigation:

NPT (nitro-blue-tetrazolium)
Screening test (neutrophil fail to release oxygen radicals which kill the microorganism)

2- Lazy neutrophil syndrome:

Chemotactic function is lost

3- Chediak-Higashi syndrome:

Degranulation function is lost all over the body (iris, neutrophils, hair…etc).

Acquired immunodeficiency

HIV +ve infection doesn' t mean AIDS
We call it AIDS once the clinical symptoms are present.
HIV (human immunodeficiency virus) is:
ssRNA from retroviridae family.

Transmission:

In pediatric age:

After excluding of blood and blood product vertical route is the most common one from HIV +ve mother.

Timing of transmission:

- ✓ Prenatal
- ✓ Natal → *commonest*
- ✓ postnatal

We can decrease incidence of vertical transmission by:

1- Giving the mother anti-retroviral treatment
2- Caesarian section before labor because most of infection occurs after rupture of membrane.

Clinical:

- Asymptomatic at birth
- Later on non-specific: LAP, hepatosplenomegaly.
- Recurrent bacterial infection
- Persistence malaise
- Recurrent chronic parotid swelling.
- CNS → *encephalopathy.*
- Failure to thrive
- Chronic diarrhea

Type of infection:

Opportunistic infection: like

Pneumocystis carinii.
Candida
Toxoplasmosis
In addition to regular bacteria

The early the diagnosis the better the prognosis.

Investigation:

Serology is useless (any serology or western plot before 18 months of age is not diagnostic)

Treatment:

Supportive measures.

Vaccination.

Life attenuated vaccines are contra-indicated

But sometimes it is classify to mild, moderate, and severe in which life attenuated vaccines are contra-indicated.

Poisoning

General measures in any case of poisoning: top priority

1- Prevent more exposure
   E.g. CO poisoning where you will lie next to him if you don' t prevent exposure
2- CPR (resuscitation) A, B, C, D, E, F
   Then do special measure for each poisoning except in (COCO):
      1- **C**O poisoning → *hyperba*ric O_2
      2- **O**pioid poisoning → *naloxone*
      3- **C**yanide poisoning → *amyle nitrate*
      4- **O**rganophosphate → *atropine*
      In this list we have to give antidote simultaneously with resuscitation.
3- Wash skin:
   E.g. organophosphate where absorption through the skin
4- Prevent absorption:
   a- serum ipecac:
      Induction of vomiting (emesis)
      Contra-indicated in four or five situations: (***C***s)
         1- ***C***oma
         2- ***C***onvulsions
         3- ***C***orrosives
         4- Hydro***C***arbon
      In these cases we do intubation (with cuff) to prevent aspiration and do gastric lavage
      Note: don' tthrow the aspirated fluid away because of medicolegal issues.
   b- Activated charcoal:
      Adsorbent for substances which leads to excretion.
      Useless in heavy metal, hydrocarbon and corrosives.
   c- Enhance bowel movement
      E.g. Carbex (SELEGILINE)
5- Dialysis:
   Severe marked **SALICYLATE** poisoning
   Theophylline
   Methanol Ÿ ŷ intoxication can cause:
      Optic atrophy
      Severe intractable metabolic acidosis
6- Alkalinization of urine:
   e.g. Salicylate
      Phenobarbital

I- Food poisoning

When to say it is food poisoning or just a simple infection?

Food poisoning when you have 2 or more candidate carry same symptoms

1- Salmonella infection:

Many subtypes the non-typhoidal salmonella is the most common type that cause food poisoning

Ex: salmonella typhimurium

Found in poultry and eggs

I.P: 20-48 hrs

- Clinical :

  Start by diarrhea which is bloody usually then vomiting and abdominal pain.

- Treatment:

  Self limited disease but may need antibiotic in three situation:

  1- Infant less than 3 months of age
  2- Immunocompromised or on chemotherapy.
  3- Severe clinical manifestation.

2- Staphylococcus food poisoning

Not infection but toxins

I.P: 1-4 hrs

- Clinical:

  Start by anorexia and vomiting then abdominal pain and diarrhea

- Treatment: no antibacterial

  Only symptomatic measures like rehydration

3- Botulism:

Found in poor caned food

We acquired infection by two ways:

1. Exposure to spores *clostridium botulinum*
2. Toxins which inhibit Ach release (Ach neurotransmitter for all muscle and CNS and autonomic system except sympathetic) so cause paralysis and life threatening respiratory dysfunction.

II- Selective poisoning

1-CO poisoning:

- Source:
  Incomplete burning like car fumes
  In closed area where warming by burning wood and no fresh air so O_2 consumed and become insufficient to make CO_2 so incomplete burning start to be produce CO.

The problem with CO that the affinity toward Hb is 200 times the O_2 which lead to tissue hypoxia.

- Treatment:
  Hyperbaric O_2

2-Acetominophen (paracetamol):

Cause liver toxicity.

Nomogram to see toxicity level after 4 hrs.

If it is in toxic range we have to give the antidote N-acetylcysteine (orally)

Gastric lavage after 4 hrs from ingestion is questionable because the physiological gastric emptying takes place within 4 hrs.

► Note: (paracetamol is a tricky drug)

Liver failure may need time to develop even after resolution of all symptoms so be careful.

3-Salicylate (Aspirin) poisoning:

Rheumatoid arthritis and rheumatic fever patient now are the most susceptible because of the high doses they take. E.g.

Rheumatic fever take 100-125mg/kg

Therapeutic range 10-20

Toxicity level >20 which is so close to the therapeutic level.

- Clinical
  1st respiratory alkalosis due to respiratory irritation
  Then metabolic acidosis
- Treatment:
  - No antidote.
  - Hydration
  - Alkalinization on the urine → *increase PH so increase* its excretion but be careful K, Na loss.

4- Iron poisoning:

Most of cases between 2-6 years old because:

Most of mothers take iron supplement and the color of the tablets is brown (like chocolate)

- Pathology:
  1st gastric ulceration, pyloric stenosis, hematemesis
  Systemic effect
  Radiopaque in early X-ray after ingestion.

- Treatment
  Antidote: Deferoxamine we give it when: Serum Fe → *300*
  Serum Fe > TIBC
  Note it cause red urine

5- Tricyclic antidepressant:

- Clinical:
  Anticholinergic effect: urine retention
  Tachycardia
  Mydriasis
  Convulsion with higher doses
  Arrhythmia: supraventricular, ventricular tachycardia or fibrillation
- Treatment:
  Alkalinization
  Physostigmine in case of intractable arrhythmia
  Diazepam for convulsions.

6- Corrosive (Alkalis, acidis):

Affect the GIT from lips, mouth

In esophagus the burns heal by fibrosis which end by stricture (dysphagia)

Alkaline burn is more severe than acid because of liquifactive necrosis (through all layer)

E.g. drain cleaner:

Treatment: never induce emesis.

Give water, milk or any thing to dilute it.

Schedule patient for endoscopy to evaluate the burns and it's extending.

7- HydroCarbons:

Gasoline (Benzine): has a systemic effect

Cardiac toxicity, arrhythmias (fibrillation)

Gasoline abuse: Through smelling (like pettix) which result in:

- White matter atrophy
- Hallucinations, and euphoria
- Ataxia
- Life threatening cardiac effect (increase sensitivity of myocardium to adrenaline so any stressful situation can end by death)

Kerosene: has a local effect

- Pneumonitis → *b/c of aspiration*
- By X-ray shows infiltration associated with fever
- Characteristics smell
- Contraindicated to do emesis

8- Lead poisoning:

- Source:

  Old paints
  Factories
  Cement

- Clinical:

  Recurrent abdominal pain (similar to VOC in SCD)
  Anemia: microcytic hypochromic (DD →*Iron, thalassemia* and sideroblastic anemia)
  Encephalopathy
  Mental retardation
  Convulsions

- Antidote:

  EDTA (ethylenediaminetetraacetic acid)

9- Mercury:

- Source
  Factories
- Clinical
  Inhalation→ pneumonitis
  Oral→ *stomatitis, gastritis, renal involvement*

10- Rat poisoning:

It is Warfarin with purple color tablets which make it danger for children

- Clinical
  Coagulopathy and bleeding
- Antidote: vitamin K

11- Organophosphate:

Cholinesterase inhibitor

- Clinical:
  Convulsions,
  Salivation
  Lacrimation
  Myosis
  Urination
  Defecation
  Even pulmonary edema

- Antidote:
  Atropine

12- Antihistamine (antitussive)

Anticholinergic effect (like atropine)
Dry secretion and mucous membrane, Mydriasis.

13- Digoxin:

Cause arrhythmia

- Antidote:
  Digibind

Viral hepatitis

► **Important definitions:**

Acute hepatitis:

Inflammation of liver that regress in less than 6 months.

Chronic hepatitis:

Any hepatitis lasting for 6 months or longer.

Fulminant hepatic failure:

Severe hepatic failure in which encephalopathy develops in under 2wks in pt with a previously normal liver.

Hyper acute hepatic failure:

In which encephalopathy develops in 1wk after onset of hepatitis.

Acute hepatic failure:

In which encephalopathy develops in 1month after onset of hepatitis.

Sub acute hepatic failure:

In which encephalopathy develops in 3month after onset of hepatitis.

► **Viral hepatitis**

There are many microbes that cause Hepatitis but during this tutorial we will concentrate on Viral hepatitis only.

Viral hepatitis: types

A, B, C, D, E and G

See the table

Table:

Hepatitis	Hepatitis A virus	Hepatitis B virus	Hepatitis C virus
Group	Enterovirus (RNA)	Hepadna (DNA)	Flavivirus (RNA)
Symptoms & signs	• Initially non specific: Nausea, Vomiting & Fatigue. • Abdominal pain with active hepatitis. • Jaundice & Dark urine (not always). • Diarrhea, Light colored stools (pale). • Loss of appetite. If severe: • Encephalopathy, increase jaundice & increase PT.		
Investigation	LFT, PT,CBC, Serology	Serology LFT, PT,CBC,	Serology? LFT, PT,CBC,
IP	4 weeks	4-20 weeks	2-26 weeks
Transmission Fecal - oral Blood Saliva Sexual(adult) Vertical	 Yes Uncommon Yes Uncommon No	 No Yes Yes Yes **Yes***	 No Yes Yes Uncommon Uncommon
Self-limiting	Yes	No	No
Chronicity	Never	Common + HDV	Commonest
Vaccine**	Yes	Yes	No

*from infected mother (+ve HBsAg).

1- Hepatitis A virus:

The commonest cause of hepatitis in pediatric age group more than B and C.

- Clinical presentation
  Most of childhood cases (<5 yrs) are asymptomatic (no jaundice) even +ve IgG
  1- Jaundice
  2- Fever
  3- Lethargy
  4- Loss of appetite
  5- Vomiting

- Diagnosis:
  By full history (+ve contact with infected member)
  Proper clinical examination and serology (+ve IgM)

- Investigations:
  - ✓ LFT and

    Liver enzymes aspartate aminotransferase (AST) is also known as serum glutamic oxaloacetic transaminase (SGOT); and alanine aminotransferase (ALT) is also known as serum glutamic pyruvic transaminase (SGPT). To put matters briefly, AST = SGOT and ALT = SGPT. Where ALT is more specific than AST for liver cell damage.

  - ✓ Serum bilirubin

    Note: clinically we can have (for clever student) an impression whether direct bilirubin or not

    Direct → Dark yellow (orange)

    Indirect → Golden yellow (lemon)

  - ✓ Note:

    When ever you get low or near normal liver enzymes (in hepatitis patient) and increasing bilirubin always think about fulminant hepatitis.

  - ✓ PT (prothrombin time)

    Due to decrease liver synthesis capability of coagulation factors especially factor VII which has the shortest half life

  - ✓ Serum ammonia:

    For Encephalopathy.

- Management:
  - Symptomatic for vomiting, fluid (no food restriction at all please)
  - Coagulopathy: fresh frozen plasma.
  - High serum ammonia: dialysis, lactulose

- Prevention:
  - Isolation till symptoms subside
  - Good food hygiene
  - The problem with HAV is the most infectious period is the week before symptomatic stage.

- Vaccination:
  - Inactivated virus given at 2 years old is highly immunogenic and if we give another shot after 6 months will give 100% immunity.
  - Immunoglobulin :
    Given after exposure within two weeks if after 2 wks will not benefit.

2- Hepatitis B virus (HBV)

In paediatric age group Transmission mostly through infected mother

- Clinical presentation:
  Mostly asymptomatic
  Serum sickness like syndrome (skin rash and arthritis), anorexia, jaundice, right upper quadrant discomfort, lethargy.

- Diagnosis:
  By serology
  It consists of inner core and an outer surface capsule:
  Inner core is formed of core protein (HBcAg). Core protein contains DNA and DNA polymerase.
  Capsule protein is referred to as (HBsAg).
  HBV also contains (HBeAg).
  - ✓ HBsAg → *indicate active infection*
  - ✓ HBeAg → *highest infectivity*
  - ✓ Anti HBc → *indicate* current or past infection
  - ✓ Anti HBs → *Immunity; previous exposure (as in* vaccinated child with no previous infection).
  - ✓ Anti HBe → *Seroconversion*

- Treatment:
  Interferon
  Monitor:
  Liver enzymes.
  PCR
  Biopsy as baseline for pathology

- Vaccination:
  - 3 doses ideally at birth, 2nd month and 6th months of age (if missed any shot you can complete the doses)

- Infant of +ve HBsAg mother:
  Should receive the vaccination as other babies in addition to immunoglobulin as early as possible (in separated syringe).
  We have to check in the child develops Anti HBs (we don' t screen normal infant for Anti HBs)

➢ Complication:
Fulminant hepatitis
Chronicity increases as the age decreases i.e. infants of +ve HBsAg mother have the highest risk to develop chronicity.

3- Hepatitis C virus (HCV)

➢ Clinically:
Large percentage is asymptomatic
85% will develop chronic hepatitis 25% of them will have cirrhosis and hepatocellular carcinoma.

➢ Investigation:
Immunological window:
Persons with early infection may not as yet have developed antibody levels high enough that the test can measure
So do PCR

➢ Treatment:
Combination therapy with pegylated interferon and ribavirin is the treatment of choice resulting in sustained response rates of 40%-80%
Monitor:
Liver enzymes.
PCR
Biopsy as baseline for pathology

➢ No vaccination
➢ Complication:
After 20 years cirrhosis and hepatic cellular carcinoma.

4- Hepatitis D virus (HDV)

Come with or over HBV
Lead to increase risk of fulminant hepatitis and the rate of chronicity.
Detected by Anti D virus.

Note:
Whenever you have fulminant hepatitis B rule out co- or superinfection of hepatitis D virus.

5- Hepatitis E virus (HEV)

Feco-oral transmission
No chronic stage

6- Hepatitis G virus (HGV)

Most of the cases are sub clinical.
If present alone its significant is questionable.

INFANT FEEDING

- Nutritional requirement
- Fluid requirement
- Electrolyte requirement
- Breast feeding
- Formula feeding
- Weaning
- Total parenteral nutrition

➲ Adequate nutrition is essential to
- Maintain body mass
- Support activity and play
- Allow growth and development

➢ INFANT NUTRITION

♦ NUTRIENT
- Macro nutrients—CHO, Lipid, Protein
- Micro nutrients
  - Vitamins-fat soluble (A,D,E,K),water sol(B,C)
  - Minerals-Na, Cl, K, Ca, Ph, Mg
  - Trace Elements-Fe, Zinc, Iodine, Copper, Fluoride, selenium, Manganese, Chromium

♦ Nutritional requirement
- Infant 110 Cal/kg/day
- 1-3 yrs 100 Cal/kg/day
- 4-6 yrs 90 Cal/kg/day
- 7-9 yrs 80 Cal/kg/day
- 10-12yrs 70 Cal/kg/day
- 13-15 yrs 60 Cal/kg/day

♦ FLUID REQUIREMENT
- 1st 10 Kg body Wt 100 ml/kg
- 2nd 10 Kg body Wt 50 ml/kg
- For each additional Kg 20 ml/kg

Body surface area Method: 1500 ml/m^2/24hr

- ELECTROLYTE & MINERALS REQUIREMENT
  - Sodium 2-3 mEq/kg
  - Potassium 2-3 mEq/kg
  - Chloride 2-3mEq/kg
  - Calcium 0.5-1.5 Gm/day
  - Phosphorus 0.5-1.5 Gm/day
  - Iron 6-15 mg/day
  - Iodine 6-15 mg/kg/day

- Sources of Calories
  - Carbohydrate 50-55%
  - Fat 30-35%
  - Protein 10-15%

  Calories utilization
  - BMR 50% Physical activity 25%
  - Growth 12% Faecal loss 8%
  - Specific dynamic action of food 5%

- Principles of feeding
  - Feed according to expected wt
  - GIT should be used whenever possible
  - Milk should not be diluted after 12 weeks of age
  - No sugar should be added to the bottle feed
  - Weaning food should be started at 4-***6*** mo

- Breast Milk vs. Cow Milk

	Breast Milk	***Cows Milk***
Calories	67	67
Water	87%	87%
CHO(lactose)	7 Gm/dl	4.8Gm/dl
Fat	3.8 Gm/dl	3.8Gm/dl
Protein	1.1Gm/dl	3.3Gm/dl
Lactalb:cas	60:40	20:80
Na(mEq/L)	7	25
K (mEq/L)	14	35

Breast is best?
- Anti-infective properties
- Humoral-Secretory IgA, Bifidus factor, Lysozyme, lactoferrin, interferon

- Cellular-Macrophages (phagocytic, synthesis lysozyme,lactoferrin,C3,C4)
- Lymphocytes-T-cell transfer delayed hypersensitivity response to infant, B cell synthesize IgA

♦ **Nutritional properties**

Protein quality-more easily digested curd (60:40 whey:casein ratio)

- Hypoallergic—reduce atopy, eczema, asthma
- Lipid quality-rich in oleic acid-improved digestibility & fat absorption
- Breast milk lipase-increased lipolysis
- Calcium: phosphorus ratio 2:1 prevents hypocalcaemia tetany & improve calcium absorption
- Low renal solute load
- Iron content bioavailability (40%-50% absorption)
- Emotional-promote close attachment between mother and baby
- Reduction in disease occurrence in later life-reduce incidence of IDDM, SIDS, Otitis media, inflammatory bowel disease, eczema, necrotizing enterocolitis (NEC), respiratory infection, urinary tract infection
- Maternal Health-promote involution of uterus, reduction in breast cancer, ovarian cancer

♦ **UNICEF Ten Step to successful breast feeding**

1. Written breast feeding policy
2. Train all healthcare staff
3. Inform all pregnant women about benefits
4. Help mother initiate BF soon after birth
5. Show mother how to breast feed and how to maintained lactation even if they are separated from babies
6. Give newborn no food or drink other than BM unless medically indicated
7. Practice rooming in, allowing mother & infant together 24hr a day
8. Encourage breastfeeding on demand
9. Give no artificial teats or dummies
10. Establish BF support group

www.babyfriendly.org.uk

- Supplement to Breast Fed Infant
  - Give Vit K1 to all babies(1mg Vit K)
  - Give Vit D to all breast fed babies(400 IU/day)
  - Give Iron to all breast fed babies by 6 mo

- Disadvantages of Breast Feeding
  - Unknown intake-volume of milk
  - Transmission of infection-CMV, hepatitis, HIV,TB
  - Breast milk Jaundice-mild self limiting
  - Transmission of drugs-antithyroid, anti cancer
  - Nutritional inadequacies-prolong BF without introduction of solids lead to poor weight gain, rickets
  - Vit K deficiency—hemorrhagic disease of newborn
  - Less flexible, emotional upset if unsuccessful

- Infant formulas
  - Term formula-Similac,Nan,S26
  - Preterm Formula-Similac special care
  - Soy based Formula-Isomil
  - Lactose free formula, Lacto-free
  - Fructose free, Similac
  - Glucose free formula, Galactomin
  - Protein hydrolysate formula, Nutrimagen
  - Elemental formula, Progestamil

- Weaning
  - Gradual introduction of food other than breast milk or formula
  - Aim to increase the energy density of diet and provide iron , vitamin, trace mineral
  - First iron fortified infant cereal, next strained fruits & vegetables progressing to pureed meats & fish
  - Allergic items (egg whites, chocolates)are not recommended till first 1st yr
  - Whole cow milk not until 1 year

  ONSET: Weaning not earlier than 4 mo & not later than 6 mo

Take Home Message?
Breast is the best

FAILURE TO THRIVE

- Persistent weight below 3rd percentile or falling off the growth curve

- **FTT Causes**
  Non organic
  Organic

A- FTT-Non organic causes

- Feeding Problem-insufficient breast milk or poor technique
- Maternal Stress-malnourished, Tense
- Financial difficulties
- Lack of stimulation & undernutrition
- Munchausen' s syndrome by proxy

B- FTT-organic causes

1) Inability to feed
   - Mechanical Problem-cleft palate
   - Lack of coordination-cerebral palsy

2) Poor retention of food
   - Vomiting
   - Gastro-esophageal reflux

3) Illness induced anorexia
   - Cystic fibrosis
   - Renal failure
   - Congenital heart disease

4) Malabsorption
   - Celiac disease
   - Cystic fibrosis
   - Cow milk protein intolerance

5) Increased energy requirement
   - Cystic fibrosis
   - Malignancies

6) Metabolic
   - Hypothyroidism
   - Amino acid & organic acid disorder, IEM

7) Infection
- TB,HIV
- UTI
- Intestinal parasites
- Gastro enteritis(chronic)

8) Mixed
- Chromosomal disorder
- Syndromes
- Immunodeficiency
- Resp. failure

♦ **FTT-History**
- Family history
- Birth Hx
- Feeding Hx
- Maternal anxiety
- Detail of vomiting, diarrhea, stool color,
- Travel-foreign, domestic ect.

♦ **FTT-Physical Exam**
- Growth Chart-Wt, Ht. & HC
- Development Assessment
- Wasting of buttock & thigh
- Dysphorphism
- Pallor
- Cleft palate
- Heart murmur, cracks

♦ **FTT- Investigations**
- CBC, CRP
- RFT
- LFT, ferritin.
- Immunoglobulins
- Anti-endomysial & antigliadin
- Urine
- Stool
- Chest X-ray-sweat test

- **FTT-Management**
  - Non organic-multidisciplinary
  - Organic-dietician, admission in ward?

- **FTT-Key Points**
  - Consistent Wt below 3rd percentile and falling off the growth curve are both evidence of FTT
  - Most cases are non organic
  - Any organic system may be implicated in organic FTT
  - Think broadly for differential diagnosis

- **FTT-Take home message**

***Failure to thrive is a* description**

Not a diagnosis

MALNUTRITION

- NUTRITION
  - An adequate diet is essential to:
    - Maintain body mass
    - Support activity and play
    - Allow growth and development
  - Nutrient adequacy can be evaluated by
    - Dietary history
    - Exam of growth data and physical exam
    - Laboratory testing

- NUTRIENTS
  - **Macro Nutrient(calorie)**
    Carbohydrate, Lipids, Protein
  - **Micro Nutrient (Non calorie)**
    Vitamins----------Fat sol.(A,D,E,K)
    Water sol. (B,C)
    Minerals----------Na, Cl, K, Ca, Ph, Mg
    Trace Elements-----Fe, Zn, Iodine, Copper, Fluoride, Selenium, Manganese, Chromium

- CALORIC REQUIREMENT

Age	***Calories***
Infants	110 cal/kg/day
1-3 yr	100 cal/kg/day
4-6yr	90 cal/kg/day
7-9yr	80 cal/kg/day
10-12yr	70 cal/kg/day
13-15yr	60 cal/kg/day

  - *Caloric requirement increase in fever, cardiac disease, major surgery, severe sepsis, burns!*

- Source/supply of calorie
  - Sources

Carbohydrate	50-55%
Fat	30-35%
Protein	10-15%

- Supply

BMR	50%
Physical activity-	25%
Growth	12%
Fecal loss	8%
Specific dynamic action	5%

➢ FLUID REQUIREMENT
- **Holliday-Segar method:**
  - 1st 10 Kg body Wt= 100ml/kg
  - 2nd 10 kg body Wt= 50 ml/kg
  - For each additional Kg= 20ml/kg
- **Body Surface Area Methods:**
  - 1500 ml/m^2/24hrs

➢ Electrolytes/Mineral Requirements
- SODIUM 2-4 mEq/kg
- Potassium 2-3 mEq/kg
- Chloride 2-3 mEq/kg
- Calcium 300mg/kg
- Phosphorus 1 mmol/kg
- Vitamins

  Vit A 1500-5000 IU/day

  Vit D 400 IU/day

➢ INFANT FEEDING
- The gastro intestinal tract should be used whenever possible—safer, Easier, Less septic and metabolic complications
- Breast feeding is the best
- Small bowel feeding must be by continuous infusion
- Elemental diet are useful with limited enteral function
- Continuous enteral drip feeding is better tolerated than bolus feeding when there is gastric emptying delay or severe enteral damage
- TPN for unstable

➢ Protein/Energy MALNUTRITION (PEM)

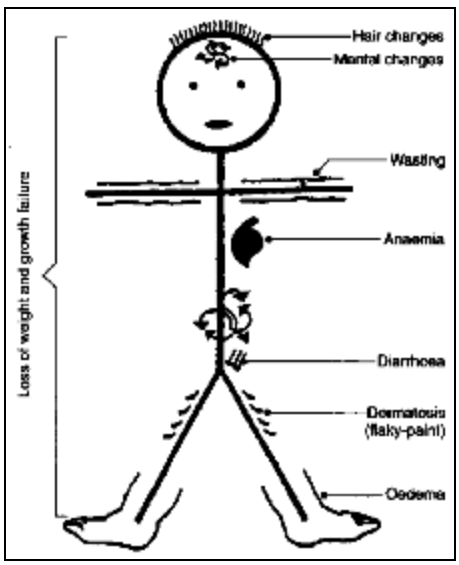
- Malnutrition is defined as a pathological state resulting from relative or absolute deficiency of one or more essential nutrient.
- Common in children between age of 3mo and 3yr
- Cause of mortality
- Malnutrition in infants and preschool children may effect growth & development

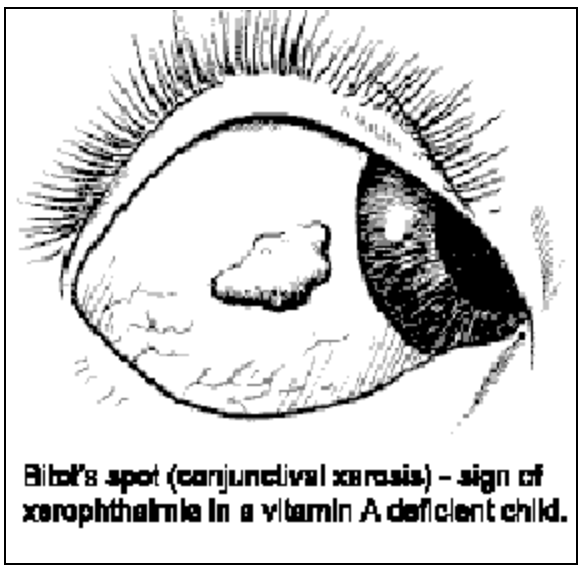
➲ MARASMUS

- *Malnutrition is due to severe **caloric** depletion*
- Emaciation with body weight <60% expected for age
- Loss of muscle mass and subcutaneous tissue
- Skin is dry and thin
- Hair is thin and sparse
- Weakness and hypotonia

➲ KWASHIORKOR

- *Malnutrition is due to inadequate **protein** intake*
- Edema with body wt from 60-80% of the expected for age
- Loss of muscle mass
- Skin changes from hyperpigmented hyperkeratosis to an erythematous macular rash
- Hair is sparse easily pluckable and appear dull brown
- Irritability and secondary immunodeficiency





Bitot's spot (conjunctival xerosis) – sign of xerophthalmia in a vitamin A deficient child.

- Causes of PEM
  - Primary Malnutrition
    - Failure of Lactation
    - Ignorance of weaning
    - Poverty
    - Cultural Pattern and food fads
    - Lack of immunization and primary care
    - Lack of Family Planning
  - Secondary Malnutrition
    - Infections
    - Congenital Diseases
    - Malabsorption
    - Metabolic disorder
    - Psychosocial

- CLASSIFICATION OF PEM
  - Gomez Classification
    - Ist degree : If wt is 75-90% of expected wt
    - 2nd degree: If wt is 60-75% of expected wt
    - 3rd degree: If wt is <60% of expected wt
    -
  - Waterlow Classification

	WT for Age		
HT for age	***Below 80%***	***Bet 80-119***	***>120%***
< 90%	Ch Malnut	Stunted grow	Obese/Stunted
> 90%	Ac Malnut	Normal	Obese

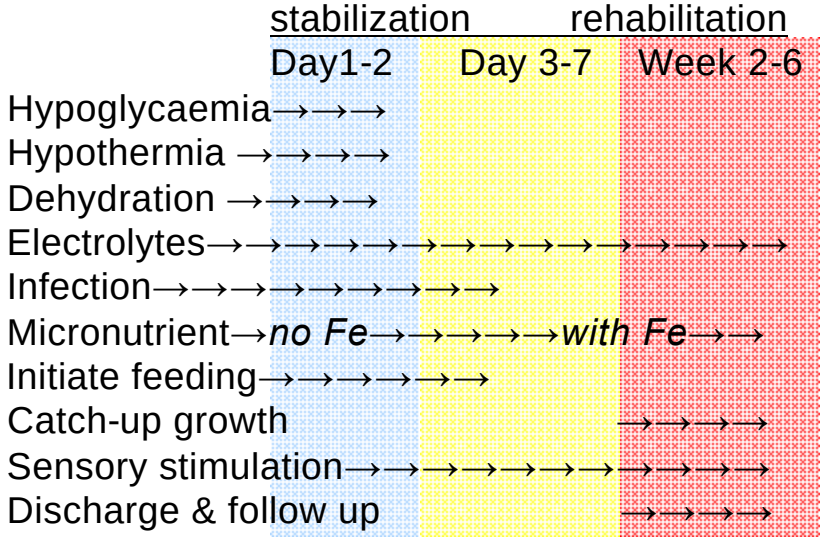
  - General Classification PEM
    - Mid-Arm Circumference:
      1yr =16.5cm
    - Skin fold: by Caliper in region of triceps or back of shoulder
      Normal = 9-11mm
    - Quadriceps Strip: with special tape with colors:
      Up to green color → Normal .
      Yellow color → Borderline malnutrition
      Red color → Malnourished .

- Assessment of PEM
  - History
    - Recent intake of food and fluids
    - Usual diet (before the current illness)
    - Breast feeding
    - Duration and frequency of diarrhea/vomit
    - Loss of appetite
    - Family circumstances
    - Chronic cough
    - Contact with TB
    - Recent contact with measles
    - Known or suspected HIV infection

  - Examination
    - Sign of dehydration
    - Shock
    - Oedema
    - Severe palmer pallor(anaemia)
    - Eye sign of vit. A deficiancy; Bitot' s spots
    - Localising sign of infection
    - Sign of HIV infection
    - Fever or Hypothermia
    - Mouth ulcers
    - Skin changes of Kwashiorkor

- Management of PEM
  - Acute management of shock, infection, hypoglycaemia, anaemia, dehydration
  - Initial stabilization and rehabilitation phase

  - ***Time framework for management of PEM***



Note:
Iron therapy usually is not started until final phase of treatment so as to prevent binding of iron to already limited stores of transferrin, which, in turn, may interfere with the protein's host defense mechanisms. There also is concern that free iron during the early phase of treatment may exacerbate oxidant damage, precipitating clinical kwashiorkor or marasmic kwashiorkor in a child with clinical marasmus.

- Initial Refeeding (PEM)
  - Frequent small feed of low osmolality & low lactose
  - Oral or nasogastric feeds
  - 100Kcal/kg/day
  - Protein:1-1.5g/kg/day
  - Liquid: 130ml/kg/day(100ml/kg if oedema)
  - Continue breast

- Catch-up growth (management PEM)
  - Return of appetite and loss of oedema
  - After a gradual transition ,give
    - Frequent unlimited amount
    - 150-220 Kcal/kg/day
    - 4-6 g of protein/kg/day
    - Continue breast feeding
  - Avoid causing heart failure
  - Assess progress
  - Treat associated condition
    - Eye problem, severe anaemia, skin lesion
    - Diarrhoea (giardiasis, lactose intolerance, osmotic diarrhea)
    - Tuberculosis, HIV, psychosocial problems

NUTRITIONAL RICKETS

- Failure of mineralization of growing bone due to Vit. D deficiency
- Common in tropics and subtropics due to poor dietetic intake of vit. D or lack of sunshine.
- Disease of rapidly growing bones and usually occurs in the first 2 year
- Vit. D participate in the absorption of:
  - calcium and phosphorus from intestine,
  - mobilisation of calcium from bone and
  - reabsorption of P from kidney

- ♦ Signs of florid rickets
  - Head
    - Frontal bossing
    - Craniotabes
    - Delayed closure of fontanelle
  - Teeth
    - Delayed eruption
    - Defective enamel and caries
  - Thorax
    - Rachitic rosary
    - Harrison' s sulcus
    - Pigeon chest deformity
  - Spine
    - Kyphosis
    - Scoliosis
    - Lordosis
  - Pelvis
    - Contracted pelvis
  - Extremities
    - Widening of wrist, ankle
    - Bending of long bones—bowing & knock knee
  - Hypotonia, laxity of ligaments, short stature, tetany

- ♦ Diagnosis of Rickets
  - History of inadequate vit D intake
  - Clinical manifestation
  - Biochemistry
    - Serum calcium
    - Serum phosphorus
    - Alkaline phosphatase
  - X-ray changes: **wrist**, ankle, knee

- ♦ Treatment of Rickets
  - Inj vit D3 600,000 I.U I/M inj once
    Repeat if no evidence of healing at 2 wk
    OR Vit D 20,000 I.U orally for 1 month
  - High calcium intake
  - Maintenance therapy vit D 400 I.U for 1-2 yr

- ♦ PREVENTION OF PEM/Rickets
  - EDUCATION
  - EDUCATION
  - EDUCATION

The diabetic child

- **Definition:** syndrome characterized by disturbed metabolism of carbohydrate, protein, and fat resulting from a deficiency of insulin secretion or its function.

It is the most common metabolic disorder in childhood (about 60% of child endocrine cases are DM1)

Morbidity and mortality are due to micro and macro vascular complications and they are depending on two factors:

- Degree of metabolic disturbance
- Duration of metabolic disturbance

► **Macrovascular complication**

- Retinopathy
- Nephropathy
- Neuropathy

► **Medium size vascular complication (most common cause of death in these patients)**

- Ischemic heart disease
- Arterial obstruction with gangrene of extremities

► **Classification:**

- *Type 1DM: β*-cell destruction leading to complete insulin deficiency.
  a) Immune mediated
  b) Idiopathic
- Type 2DM: combination of insulin resistance and deficiency.
- Others (Type 3DM) Table.
- Type 4DM: gestational diabetes

► **Dx:**

➢ **Diabetes:**

- FPG ≥ *126 mg / dL (7.0 mmol / L)*
- RBS ≥ *200 mg / dL (11.1 mmol / L) + symptoms*
- OGTT: 2h PG ≥ *200 mg / dl*

➢ **Impaired fasting glucose:**

- FPG ≥ *110 & < 126 mg / dl*

➢ **Impaired glucose tolerance test:**

- 2h PG ≥ *140 & < 200 mg / dl*

➢ **Normal:**

- FPG ≤ *110 mg / dl or 2h PG < 140 mg / dl*

	DM	DM
Genetic	**Disease risk associated with specific HLA haplotype**	**Strong family clustering but a specific gene marker not identified**
Environmental	**? viral triggering autoimmune ? ingested antigens (e.g. caw milk)**	**Sedentary life style Obesity, ? drugs**
Autoimmune	**Yes**	**No**

- **Type 1 DM**
  - Epidemiology:
    - Childhood & adolescence,
    - 2 peaks: school age and 16 year of age.
    - M = F
    - Finland, Sweden, Kuwait, & Norway; have highest incidence
    - China & Japan have the lowest incidence (we don' t know why)
  - Etiology, Pathogenesis & Genetics:
    - HLA typing
    - Genetic susceptibility
    - Environmental factor/s

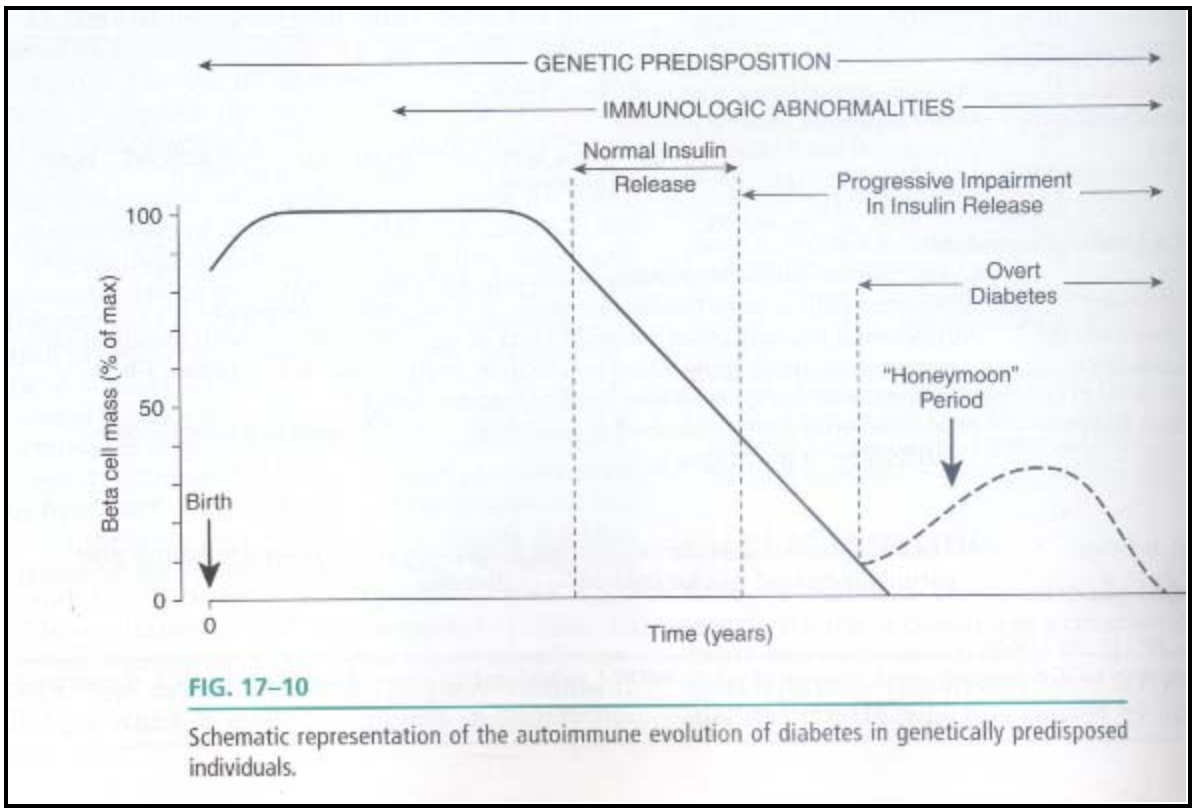


FIG. 17–10

Schematic representation of the autoimmune evolution of diabetes in genetically predisposed individuals.

- **Cumulative risk (for DM)**
  - For sibling of DM pt: is 6-10% vs. 0.6% of general population
  - For off spring of affected mother: is 2.1%, while of affected father: is 6.1%
  - If both parent are affected by DM , there is 30% chance of each child to have DM
  - For monozygotic twins: the risk is 50% (for DM the risk is 85%)

- **Clinical presentation:**
  - polyuria, 2ry nocturia, polydipsia, wt. loss, fatigue & lassitude (lethargy)
  - Associated symptoms: muscular cramps, blurred vision, frugal or bacterial infection
  - 5-10% present with diabetic ketoacidosis(DKA)

- **Complication**
  - **Acute:**
    - Hypoglycemic; coma; convulsion.
    - DKA
    - Somogy & Dawn phenomena

	Somogyi Phenomena **(Rebound Hyperglycemia)**	**Dawn Phenomena**
Pathophysiology	•Rebound hyperglycemia due to counterregulatory hormones (cortisone, GH,..) •Follows a hypoglycemic reaction during the night due to high insulin dose at night	•Waning-off of Insulin action in AM hours •Secondary to increased nocturnal GH output •Results in high AM blood sugars
Diagnosis	Check 3 am blood sugar	•Check 3 am blood sugar
Management	Decrease evening long-acting Insulin (NPH) dose	•Increase evening long-acting Insulin (NPH) dose

➢ **Chronic:**

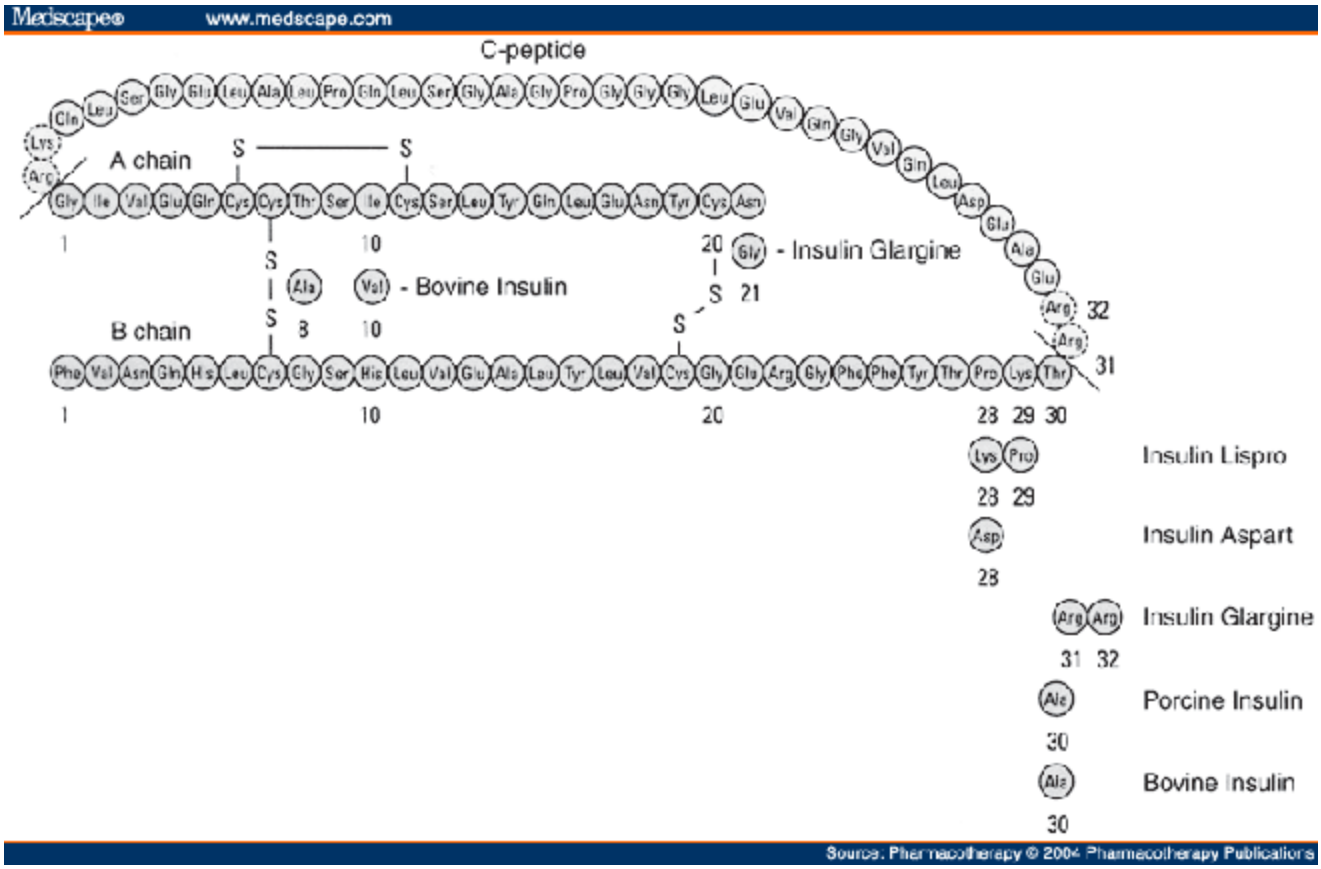
Micro & macrovascular complication

► **Islet cell structure**

B-Cells lying exactly next to the blood circulation in islet of *langerhans followed by α-cells then γ*-cells, why?

- Because the glucose level is very high in the circulation *to the extend that it can kill any type of cell (except B-*Cells) as a result of glucose toxicity
- *B*-Cells have the key for glucose uptake which is GLUT-2

► **Insulin structure:**



► **What is the importance of C-peptide?**

- It can help in differentiation between DM (low) and DM (high)
- For patient with recurrent hypoglycemia:
  - If C-peptide is high → suspecting malignancy
  - If it is low → incorrect over dose of insulin

(B/c exogenous insulin doesn' t have Gpeptide)

► **Functions of insulin:**

- anabolic hormone
- ↑ *glycogenesis*
- ↑ *glucose uptake by muscle & adipose cells*
- ↓ *glycogenolysis*
- ↓ *gluconeogenesis*
- ↓ *li*polysis

► **DKA pathogenesis:**

- absolute / near absolute insulin deficiency
- progressive hyperglycemia
- osmotic diuresis
- lipolysis ; FFA
- gluconeogenesis
- ↑ *counter regulatory hormones; glucagon, GH,* adrenalin & cortisol
- ketosis: FFA converted by glucagon & adrenalin in hepatocytes to ketone bodies

► **Cerebral edema:**

- 1-2 % of all DKA pt
- Higher incidence in children (b/c the space of the cranium is small compare to the brain mass)
- Out come is poor: 1 / 3rd die, 1 / 3rd sustained neurological deficit, & 1 / 3rd recover
- Subclinical (radiologically detected) is more common than clinical
- Can occur at initial stage of DKA but commonly occur during IVF management of DKA

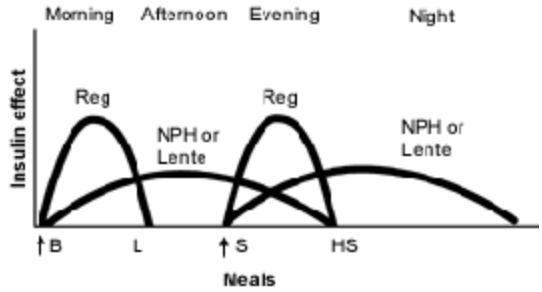
➢ **Indications for ICU admission in a patient with DKA:**

- comatose patient
- severe dehydration
- pH < 7.0
- Age less than 5 years (↑ *risk of cerebral edema)*
- Blood sugar > 1000 mg/dl
- Nurse staff is busy in the general ward

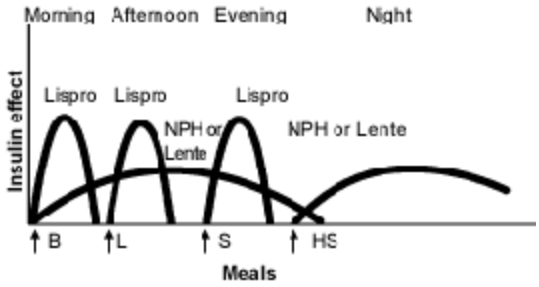
- **Out pt monitoring**
  - Home glucose monitoring
  - Hb A1c
  - Thyroid function test (5 % abnormality) & lipid profile yearly
  - Ophthalmology exam: yearly after 5y of diagnosis
  - microalbuminuria yearly after 5y of diagnosis and/or puberty

- **Management:**

  - **Regimens:**
    - Twice-daily Insulin



    - Multiple Daily Insulin Injection



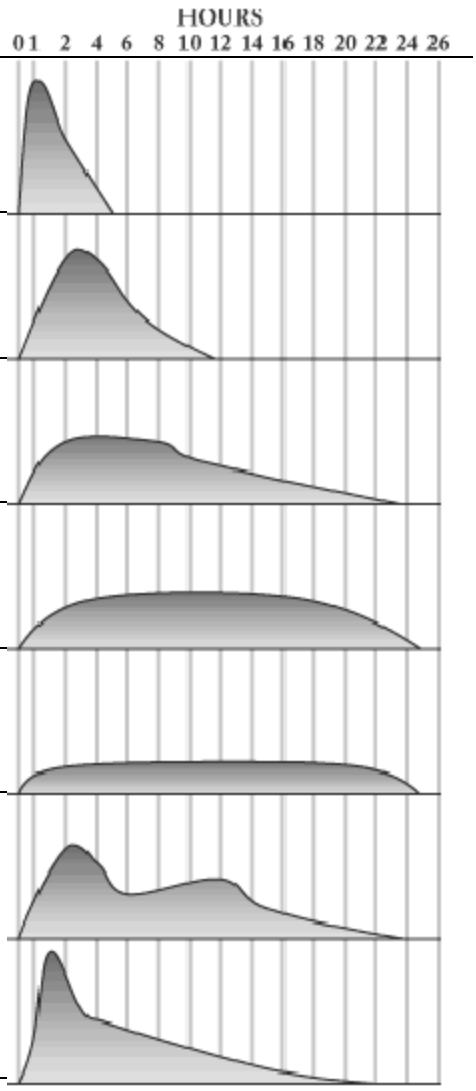
Notes:

- As the times of injection increase as the control of blood sugar will be better
- These pictures are only examples, these regimens can be done through different ways and different types of insulin

➢ Types of insulin:

Ultra-short acting insulin is used more frequent in children than short acting because children don' t restrict or fixed to aspecific time for their meals so we use ultra-short acting insulin after the meal immediately.

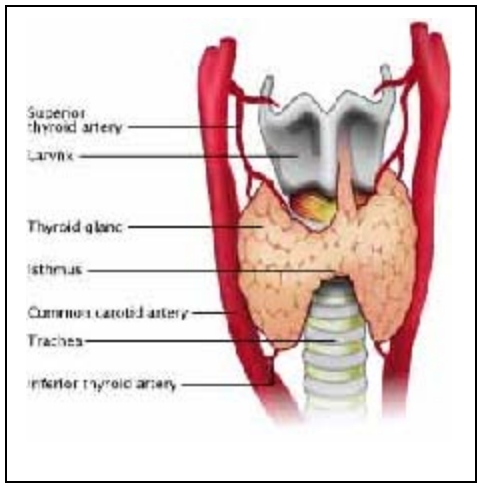
Insulin type/action	Trade names
Rapid-acting analogue (clear) Onset: 10–15 min Peak: 60–90 min Duration: 4– 5 h	Humalog® (insulin lispro) NovoRapid® (insulin aspart)
short-acting (clear) Onset: 0.5–1 h Peak: 2–4 h Duration: 5–8 h	Humulin®-R Novolin®ge Toronto
Intermediate-acting (cloudy) Onset: 1–3 h Peak: 5–8 h Duration: up to 18 h	Humulin®-N Humulin®-L Novolin®ge NPH
Long-acting (cloudy) Onset: 3–4 h Peak: 8–15 h Duration: 22–26 h	Humulin®-U
Extended long-acting analogue Onset: 90 min Duration:24 h	Lantus®* (insulin glargine)
Premixed (cloudy) A single vial contains a fixed ratio of insulin (% rapid- or fast-acting to % intermediate-acting insulin)	Humalog® Mix25™ Humulin® (20/80, 30/70) Novolin®ge (10/90, 20/80, 30/70, 40/60, 50/50) NovoRapid Mix*



Thyroid gland

الغدة الدرقية، اسمها مشتق من الدرقة و معناها الدرع في اللغة العربية)

Anatomy:



- Blood supply: The thyroid gland is supplied by two pairs of arteries: the superior and inferior thyroid arteries of each side. The superior thyroid artery is the first branch of the external carotid, and supplies mostly the upper half of the thyroid gland, while the inferior thyroid artery is the major branch of the thyrocervical trunk, which comes off of the subclavian artery. In 10% of people, there is an additional thyroid artery, the thyreoidea ima, which arises from the brachiocephalic trunk or the arch of the aorta. Lymph drainage follows the arterial supply.
- There are three main veins that drain the thyroid to the superior vena cava: the superior, middle and inferior thyroid veins.
- Parathyroid gland is lying on the posterior aspect of the thyroid gland.
  - ➲ N.B. even in total thyroidectomy the parathyroid glands are not removed
- Recurrent laryngeal nerve passes below the level of inferior thyroid artery, so this is should be taken in consideration during thyroidectomy.

Histology:

Follicular cells: which secrete T_3 and T_4
Colloid: rich in thyroglobulin, the colloidal material serves as a reservoir of materials for thyroid hormone production and, to a lesser extent, a reservoir of the hormones themselves.
Parafollicular " C" ells: secrete calcitonin which controls calcium blood levels

Thyroid embryological development:

In the fetus, at 3-4 weeks of gestation, the thyroid gland appears as an epithelial proliferation in the floor of the

pharynx at the base of the tongue between the tuberculum impar and the copula at a point latter indicated by the foramen cecum. Subsequently the thyroid descends in front of the pharyngeal gut as a bi-lobed diverticulum through the thyroglossal duct. Over the next few weeks, it migrates to the base of the neck. During migration, the thyroid remains connected to the tongue by a narrow canal, the thyroglossal duct.

Follicles of the thyroid begin to make colloid in the 11th week and thyroxine by the 18th week.

Notes:

- from the 3rd pharyngeal pouch the parafollicular cell will join the thyroid gland
- From 4th pharyngeal pouch the parathyroid glands will accompany the thyroid gland

- The definitive shape of thyroid gland will form at the age of 2 months.
- By the age of 11 week fetal T_4 can be detected
- TSH is detected at 4th month of gestation
- And by the age of 6 month fetal T_3 can be detected
- Thyroid gland weight at the birth time is about 1.5g while the adult weight is 15-20g.

Function:

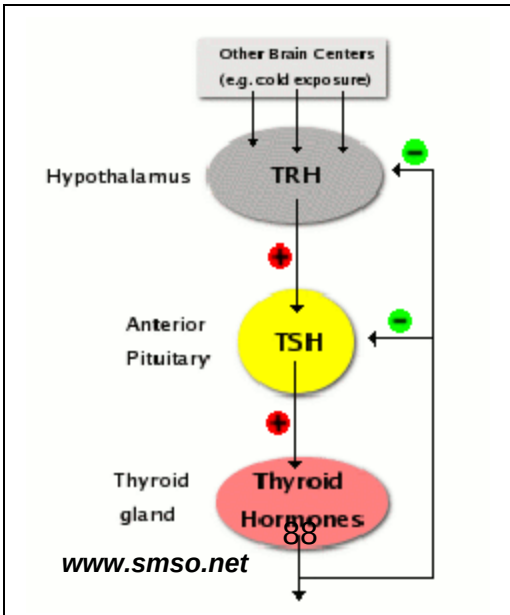
Endocrine: control system of ductless glands that secrete chemical called hormones that circulate within the body via the bloodstream to affect distant cells within specific organs.

Paracrine: form of cell signaling in which the target cell is close to the signal releasing cell.

Autocrine: form of signaling in which a cell secretes a chemical messenger that signals the same cell.

Hypothalamus pituitary –thyroid axis:

Low thyroxine production by thyroid gland will give +ve feedback on hypothalamus as well as the pituitary which make them producing more TRH and TSH respectively. This will trigger production of more thyroxine and will enhance the growth of the gland.



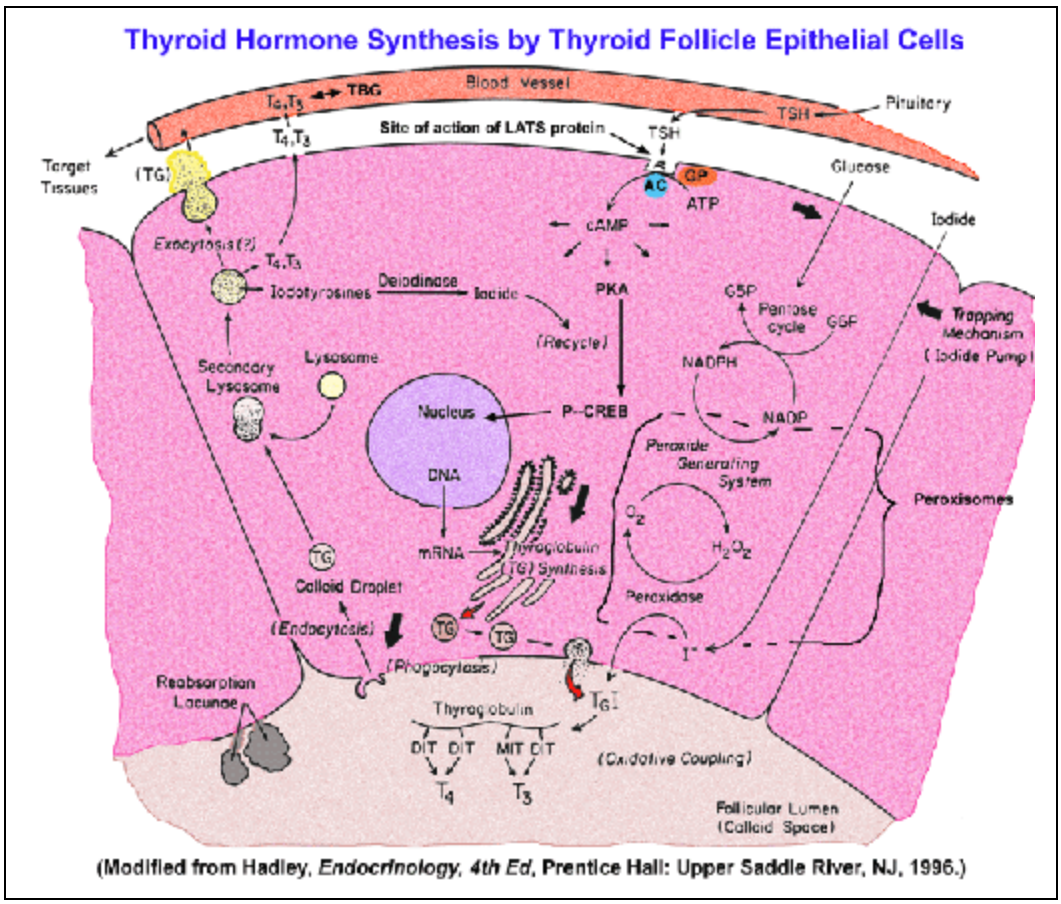
On the opposite side, high thyroxine production by thyroid gland will give -ve feedback on hypothalamus as well as the pituitary which make them producing less TRH and TSH respectively.

TSH receptor:

- Different cells have different receptors for different hormones
- TSH receptor is composed of alpha and beta unites
- The alpha unite is similar to alpha unite of LH and FSH receptors
- The difference is in the beta unit (specific unit).

Synthesis of thyroid hormone:

TSH → TSH receptor on follicular cells (it binds to the beta unit) → stimulating multiple endogenous factors → gene expression → production of thyroglobulin (TG) " protein" & hydrogen peroxide Iodine in the food is absorbed by intestine as iodide → Na – I transporter → iodide uptake (for each molecule of I, 2 molecules of Na is up taken). After oxidation of iodide into iodine by peroxidase enzyme we need Pendred's syndrome transporter to release iodine from follicular cell to the colloid to join with TG inside colloid space.



N.B. Pendred's syndrome rare autosomal recessive condition in which there is defect in Pendred's syndrome transporter so there will be uptake of iodine but without releasing it into colloid. These patients will have

- Sensorineural deafness
- Often a mild primary hypothyroidism with a non-toxic diffuse goiter

Peroxidase enzyme is responsible for oxidation of iodide into iodine then organification of iodine with thyroglobulin to form: mono-iodo thyroglobulin MIT or di-iodo thyroglobulin DIT.

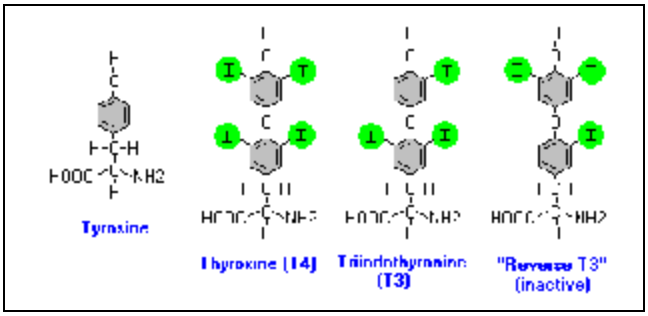
Coupling of:

mono-iodo thyroglobulin + di-iodo thyroglobulin → T_3
di-iodo thyroglobulin + di-iodo thyroglobulin → T_4

As a result, we have the large TG molecule to which T_3 & T_4 attach. They are stored in colloid space till needed. At this time, they are engulfed by follicular cells through pinocytosis " endocytosis" then T_3 &T_4 get off from TG through " hydrolysis" lysosome to be released in the circulation and the iodine in the remaining uncoupled MIT and DIT is released by the enzyme deiodinase to recycle again to be used in the synthesis of more hormones.

N.B. some time TG is released in the circulation in case of malignancy. So, TG level may be used as an indicator for thyroid tumors.

- **Structure of thyroid hormone:**
  - Internal ring: active (responsible for the action)
  - External ring



N.B. for thyroxine to be active the internal ring should be attached to two I molecules.
T_4: 2 I on the internal ring, 2 I on the external ring
T_3: 2 I on the internal ring, 1 I on the external ring (active)
rT_3: 1 I on the internal ring, 2 I on the external ring (inactive)

	Free	Total
T_3	0.3%	70-90
T_4	0.03%	?

➲ Notes:
- iodine is very important in the synthesis of thyroid hormone (64% of T4 molecular weight)
- T3 is the biologically active thyroid hormone, possessing 3-5 times the metabolic power of T4

➲ **What are the other organs that can take the iodine?**
- Thyroid 99.9%
- Salivary glands
- Gastric & intestinal mucosa } GIT
- Mammary glands
- Placenta } baby

➲ **What is the source of iodine?**
The upper layer of earth' s shell.

Daily requirement: 100 µg/day
To take this daily requirement you need to eat:
5kg of fruits & vegetables, 3kg of meat, 3kg fresh water fish, or 200-1000 g sea fish.

Endemic goiter:
In the areas where there is iodine deficiency e.g. on the mountains where the flood takeoff the iodine from the soil.
Not enough iodine for thyroid hormone synthesis → low thyroid hormone will stimulate anterior pituitary and hypothalamus to secret more TSH & TRH respectively → enlargement of thyroid gland (goiter)

Function of thyroid hormone:
- Essential to proper development and differentiation of all cells of the human body
- Control basal metabolic rate
- Increase the body's sensitivity to catecholamines
- Regulate protein, fat, and carbohydrate metabolism
- Others

Thyroid problems:

Congenital hypothyroids:

One of the causes of reversible mental retardation
Incidence: 1/2000
Screen test:
TSH: If the level =< 30 pg → normal
If 30-60 → border line → do free T_4
If > 60 pg → hypothyroidism

Treatment:
Thyroxine 50 ml
Thyroxine should be started 1 month or less after birth

Why there is mental retardation with hypothyroidism?

Brain is one of the most important organs for thyroxine to work on. It helps in:
Myelination, cell to cell communication, and neuronal development

What are the forms of goiter in pediatric?

- Simple goiter
- Physiological goiter: at pre-pubertal period because of the increase need for thyroxine.
- Goitrogenic food
- Thyroiditis:
  Acute: bacterial
  Subacute: viral (De Quervain' s thyroiditis)
  Chronic lymphocytic thyroiditis: Hashimoto' s thyroiditis.

Hashimoto' s thyroiditis:

- It is the most common thyroid problem in pediatric
- It is the most common cause of goiter in pediatric
- It is the most common cause of hypothyroidism in pediatric
- Most common in the females 4-5:1
- The patient could be euthyroid or hyperthyroid but these are rare conditions.

Clinical presentation:
Goiter
Symptoms of hypothyroidism

Investigation:

TFT (initially TSH & free T_4)

TSH ↑ and T_4 ↓ → hypothyroidism

Thyroid peroxidase antibodies

Treatment:

Thyroxine supplement

- **Grave' s disease:**

Actually Hashimoto' s thyroiditis and grave' s disease are a spectrum of the same disease. (The patient could have Hashimoto' s thyroiditis only, Grave' s disease or rarely both of them)

➲ **How to differentiate between these two diseases?**

- Thyroid stimulating immunoglobulins TSIs are only seen in grave' s disease
- Thyroid peroxidase antibodies titer is very high in Hashimoto' s thyroiditis unlike Grave' s disease in which it is +ve but no that high.

Treatment:

Anti-thyroid hormone

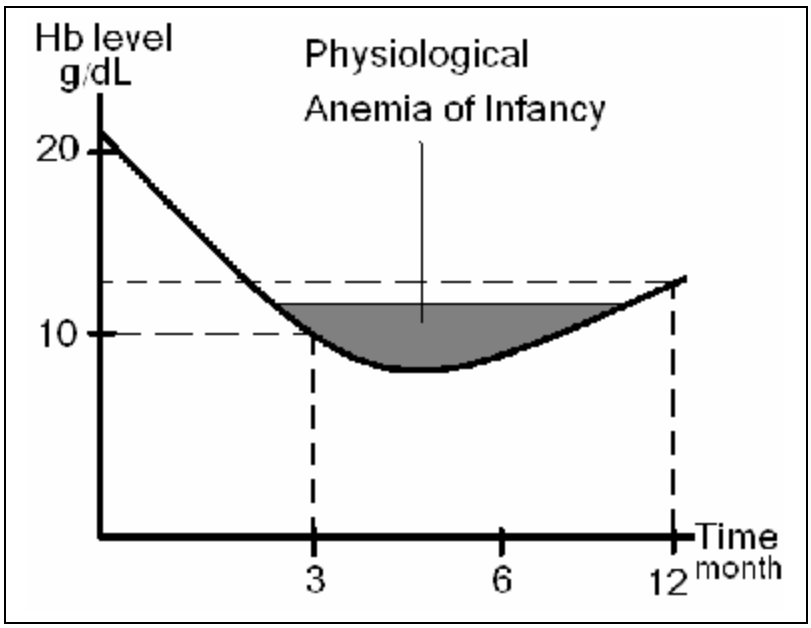
	PTU	Carbimazole
Half life	Short , (3 times/day)	12-24 h (once or twice daily)
Dose	6-10mg/kg/day	0.6-1mg/kg/day
Action	• Inhibit the release of thyroxine • Inhibit deiodinase enzyme • Inhibit coupling • Inhibit peripheral conversion of T_4 to T_3	Same but: • More potent in inhibition of coupling • Does not Inhibit peripheral conversion of T_4 to T_3

N.B. For pregnant ladies we use PTU

Child with Pallor

- ✓ **Definition of Anemia:** Hb level lower than the normal range for age & sex. e.g. Hb level of about 10 g/dL in a newborn is considered anemia, while Hb level of about 10 g/dL in a 5-month-old infant is considered normal.

Look at the graph:
Newborns have high Hb level reaching up to 20 g/dL & even more. Then it will drop to about 9-10 g/dL at the age of 3-6 months (called Physiological Anemia of Infancy). By one year of age, it will reach to the adult level.



- ✓ **What should you do if a Child with Pallor was presented to you?**

1) History:
- Prenatal: gestational age (i.e. full-term or not)
- Natal: type of delivery / was there any bleeding? / did the baby have any problem (e.g. put on ventilator / exchange blood transfusion / ...)?
- Nutritional: type of feeding (Breast-fed or Bottle-fed) / other food / amount / ... etc
  - This is the commonest cause of anemia
  - Babies only on Breast milk are liable to Iron Deficiency Anemia (especially if for >4 months)
- Past Medical History: whatever diseases after birth
- Family History: very important (inherited blood disorders)
- Review of System

Extra Information:

- Synthesis of Hb starts at the 2nd trimester. Immediately before term, Hb A synthesis starts, while synthesis of Hb F starts to decrease.

- Hb F represents 60-90% of total Hb at birth, & this level decline to adult levels (less than 5%) by 4 months of age.

2) Physical Examination:

Do complete physical examination from head to toe.

Concentrate on:

Pallor
Jaundice (hemolytic)
Nutrition (underweight or not)
Bruises (pancytopenia / Leukemia / ...)
Lymphadenopathy (Lymphoma / Leukemia)
Hepatosplenomegaly

3) Investigations:

A] CBC:

- Hb, Hct: to confirm the presence of anemia
- WBCs: may be increased as in Leukemia
- Platelets:
- Blood Indices (MCV, MCH):
  - High → Megaloblastic (B12 or Folate Deficiency)
  - Low → Iron Deficiency Anemia or Thalassemia
  - Normal → anemia of chronic disease or ineffective erythropoiesis
- Reticulocyte Count (a reflection of Bone Marrow Function):
  - Increased → Hemolytic (i.e. peripheral destruction of RBCs)
  - Decreased → underproduction
  - Normal → anemia of chronic disease

B] Blood Film: may show blast cells, abnormal RBCs (sickled, spherocyte, micro- or macrocytosis… etc)

Further Investigations:

If you suspect ...

1) Nutritional Deficiency → Serum Ferritin, or TIBC (Total Iron Binding Capacity) & Serum Iron.
2) Hemoglobinopathy → Electrophoresis
3) Bone Marrow Disease → Bone Marrow Aspiration
4) Immune disease → Coombs test

NUTRITIONAL ANEMIAS

► Iron Deficiency Anemia (IDA):

- Body stores of iron in ...
  - Premature: 0.3 gm
  - Full-term: 0.5 gm
  - Adult: 5.0 gm

- Daily Requirements of iron is 0.8-1.5 mg/day, but since only 10% of ingested iron is absorbed, amount of iron that should be present in food is about 8-15 mg/day.

- Iron is absorbed in duodenum (& partly in upper jejunum), & is present in many types of food such as green leafs, meat, cheese ... etc.

- IDA is the commonest cause of nutritional anemia.

➢ Causes:

1. Decrease intake (the commonest cause):
   Examples:
   a) A baby who is only on breast-feeding for the 1st two years of life
   b) A baby eating only one type of food such as rice
2. Decrease absorption
3. Increased loss: due to chronic blood loss e.g. drugs, polyps, infection with Ancylostoma duodenale parasite
4. Decrease iron stores: as in twins or premature babies

➢ Clinical Features:

- Mostly asymptomatic (99% of cases). So, it is discovered usually in one of two ways:
  1- The mother complains that the child is pale
  2- The doctor discovers that the child is pale during a visit for another reason
- The patient may complain of tiredness, poor concentration, headache ... etc.
- If the Hb level is <4 gm/dL, the patient may complain of palpitation & may go into heart failure.
- There is no hepatosplenomegaly or lymphadenopathy
- In chronic cases, the body of the patient is adapted to low levels of Hb without symptoms.

➢ Diagnosis:

1] History & Physical Examination:

2] Laboratory:

- Decreased Hb, decreased MCV & MCH, & decreased Reticulocyte Count.
- To confirm the diagnosis, do Serum Ferritin.

N.B: we may do TIBC & Serum Iron, but they are inaccurate because the latter is subjected to diurnal changes.

➢ Management:

1) Iron Supplement:

- There are many preparations (e.g. ferrous sulphate)
- Dose: 4-6 mg/Kg/day
- Duration: 4-6 weeks
- Once the patient start iron regimen, erythropoiesis increases → increased Reticulocyte Count (so, if you do Reticulocyte Count after 72 hours, you will find it elevated).
- After 1 week, Hb level will start to rise.
- If after 1 month the Hb level doesn't increased, either:
  - Wrong diagnosis, or
  - The patient is not compliant

2) Education about types of food containing iron.

➢ Prognosis: good

► **Folate Deficiency:**

- Absorption in jejunum (so any problem there may lead to deficiency)
- Daily Requirement: 30-50 microgram/day

N.B: Primary deficiency of Folate is rare. This is because of the followings:

1) High Folate stores in the body
2) Low requirement which is present in food usually.
3) Folate is present in many food types

So, Folate deficiency is usually 2ry to another reason.

➢ Causes:

1) Decreased intake: (pure nutritional deficiency is not common except in poor countries)

2) Decreased absorption: (e.g. Giardia)

3) Drugs: (anticancer, antithyroid, anticonvulsant, antibiotics ... etc)
4) Hemolytic: (the commonest / it is due to increased demand)

- Clinical Features:
  Mostly asymptomatic

- Laboratory:
  - Decreased Hb
  - Increased MCV & MCH
  - Serum Folate
  - Bone Marrow Aspiration (if you are in doubt)

- Management:

Folate Supplement: 1-5 mg/day

- Prognosis: Excellent except if it is due to a bad disease (you have to treat the underlying cause)

► **Vitamin B12 Deficiency:**
  - Absorbed in Terminal ileum.
  - Rare because of high stores (stores present at birth are enough for 5 years after birth!!

- Causes:

1) Congenital:
   Pernicious anemia:
   - Deficiency of intrinsic factors
   - Adults may have neurological problems, but these are extremely rare in children

   2) Acquired:
   Resection of the terminal ileum

- Diagnosis: Serum B12

- Clinical Features: pallor

- Treatment: Parenteral B12 Supplement for life (because it is mostly due to congenital disease or due to resection of the terminal ileum in which the patient need parenteral supply)

- Prognosis: depend on the cause

► HEMOLYTIC ABNORMALITIES:

➢ Introduction:

- Hb A is composed of *two α* chains & *two β* chains, & represents 97-98% of the total Hb in Adulthood.
- Hb A_2 is composed of *two α* chains & *two δ* (delta) chains, & represent 2-3% of the total Hb in Adulthood.
- Hb F is composed of two *α* chains & *two γ* chains.
- The 4 genes of *α* chain are present on chromosome 16, while the genes of *β*, *γ*, & *δ* (2 genes for every one) are on chromosome 11.
- *In the β chain of Hb S, the 6th amino acid (which is* Valine) is mutated to the amino acid Glutamate (Hb S6:V → *G)*

➲ α-Thalassemia

- α is absent.
- If all *α chains are absent → incompatible with life.*
- It is a benign disease.
- 30-*40% of the population is carrying α*-Thalassemia.
- If Hb H inclusions are +ve → *α*-Thalassemia

➲ *α*-Thalassemia type II / Silent Carrier

- asymptomatic
- *One α is deleted.*
- Hb level is normal
- Normal on Electrophoresis
- The only finding is ↓ *MCV & MCH.*
- < 5% Hb H inclusions

➲ *α-Thalassemia type I / α*-Thalassemia Minor(trait)

- asymptomatic
- *Two α are deleted.*
- Hb level is slightly below normal (10-12 g/dL)
- ↓ *MCV & MCH.*
- 5-25% Hb H

➲ ***α*-Thalassemia Intermedia (HbH disease)**

- May have splenomegaly (3-5 cm below the costal margin), & slight thalassemic features.
- *Three α* chains are deleted.
- Hb level is 7-10 g/dL.
- ↓ *MCV & MCH.*
- > 25% Hb H.
- May need Blood transfusion every 3-5 years.

➲ **Hydrops Fetalis**

- *All α are d*eleted
- Incompatible with life.

➢ Diagnosis:

1) Clinical
2) CBC
3) Hb H inclusions
4) DNA Analysis with ratio between α & β to see how much deletion is there.

* A patient with the following investigations comes to you:
  - Hb H: 5-25%
  - ↓ *MCV & MCH.*
  - Normal electrophoresis.

  What is your diagnosis? (thalassemia trait)

➲ ***β*-Thalassemia**

	***β*-Thalassemia Minor**	***β*-Thalassemia Intermedia**	***β*-Thalassemia Major**
Hb A	≥*90%*	10-90%	<10%
Hb A_2	>3.5%	>3.5%	>3.5%
Hb F	4-6%	increased	The main type of Hb
Symptoms	Asymptomatic (only ↓*MCV &* MCH)	Mild to moderate splenomegaly & mild thalassemic features	Mentioned in the pathogenesis.
Management	No treatment is required	Infrequent Blood Transfusion (every one to two years)	Recurrent Blood Transfusion (Hb level will drop in 4-6 weeks in a rate of 1 g/week)

➢ Pathogenesis:

- *Absence of all β chains → accumulation of α chains →* deposition in the membrane → injury to RBCs → chronic hemolytic anemia (pallor, jaundice, …etc) → bone marrow will try to compensate (Medullary Hemopoiesis) → expansion of the bone marrow → bossing of the frontal bone, maxillary expansion, malocclusion of the teeth … etc
- Liver & spleen which were producing RBCs during Intrauterine Life, will start hemopoiesis again (Extramedullary Hemopoiesis) → hepatosplenomegaly

N.B: All cases of β-Thalassemia Major present at infancy with severe anemia (due to drop of Hb F level)
N.B: About 0.2-*0.3% of the population is carrier to β*-Thalassemia.

➢ Diagnosis:
Hb Electrophoresis

N.B: Both α- & β-Thalassemia can be diagnosed at 10-12 weeks of gestation by studying DNA.

➢ Major Complications:

1] Severe Chronic Hemolytic Anemia & its Consequences:
The patient will be weak & short. He will have delayed puberty …etc
2] Consequences of Frequent Blood Transfusion:
a- Iron Overload:
- organs mostly affected are heart & liver
- If the patient survives enough, he will have heart failure, DM, testicular problems, bronze skin, & all organs will be affected.

b- Infections

Treatment of β-Thalassemia Major:
1) Blood Transfusion (packed RBCs): in an attempt to increase Hb level to > 12 g/dL. This serve two purposes:
a- Prevention of Medullary & Extramedullary Hemopoiesis.
b- Prevention of heart failure (because the heart is weak due to chronic anemia.
2) Chelation: Deferoxamine (nowadays, it can be administered orally also)

3) Enhancement of Excretion: Vitamin C
4) Bone Marrow Transplantation:
- Best treatment (cure rate is > 60%).
- The problem is to find a compatible allogenic donor of bone marrow, since relatives are usually carriers for the disease.

➲ **δ-Thalassemia**
- - *Some times combined with β*-Thalassemia resulting in a more severe disease.
- - *Presentation is like β*-Thalassemia.

➲ **Sickle Cell Anemia**
- Qualitative Hemoglobinopathy (i.e. normal amount but dysfunctioning Hb)
- Sickled-shaped RBCs are liable to injury easily leading to hemolytic anemia.
- When the RBCs pass in the microcirculation, they don't give O_2 easily leading to hypoxia. Hyperviscosity causes slowing of circulation leading to further hypoxia & more sickling (vaso-occlusive crisis)

(1) Painful (Vaso-occlusive) Crisis
- is the major problem
- Happens mostly in bones (in which it lasts for 24-48 hours or GIT (which result in abdominal pain).

➢ Treatment:
1) Hydration
2) Analgesia (but non-narcotic): e.g. paracetamol, codeine, isoparadol, Voltaren, etc

➢ Complications of Vaso-occlusive Crises:
1) CNS:
- Depend on the site.
- Need Blood Transfusion or Exchange Blood Transfusion.

2) Acute Chest Syndrome:
- Present with chest pain usually without fever.
- May be confused to Atypical Pneumonia.
- Need Blood Transfusion.

3) Renal Papillary Necrosis

4) Priapism → Need Blood Transfusion
5) Liver, Retina …etc.

(2) Hemolytic Crisis:

- Present with jaundice.
- Need Blood Transfusion.

(3) Sequestration Crisis:

- Sudden pooling of blood in the spleen.
- Need Blood Transfusion but slowly because sometimes the blood returns to the circulation.

(4) Aplastic Crisis:

- Bone marrow hypofunction → ↓ *all blood cells.*
- Rare.
- Need Blood Transfusion

So, all types of crises are indications of Blood Transfusion in Sickle Cell patients except Vaso-occlusive Crisis.

➢ Complications of Sickle Cell Anemia:

1] Infection:

- In the past, it was the leading cause of death.
- It is due to impaired humoral immunity & hyposplenism.
- Infection with Encapsulated organisms (pneumococci, H. influenzae, meningococci, and salmonella) are 300-400 times more common than the general population.

➢ Management:

- Prophylaxis:
  a- Active: Immunization
  b- Passive: long-acting penicillin.

2] CNS:

- More liable to stroke (< 1%).
- CNS complications of Vaso-occlusive Crisis (mentioned above).

3] Renal Papillary Necrosis.

4] GIT:

- Cholecystitis

- By the age of 20 years, 30-50% of patients will have gallstones (whether symptomatic or not).

5] Endocrine: Delayed Puberty.

6] CVS & Respiratory:
- Slightly more liable to have Ischemic Heart Disease.
- Repeated Acute Chest Syndrome → hypofunction of the lung (rare).

7] Pregnant women are more prone to have abortion, stillbirth, & premature labor.

➢ Diagnosis:

1) History:
- Repeated attacks of bone & abdominal pain.
- +ve family history

2) Electrophoresis:
- If Hb S is > 45% → diseased.
- If Hb S is < 45% → trait.

Here in KSA, there are two types of Sickle Cell anemia, namely the African type (which is more severe due to lower level of Hb F & is present in the Southern region) & the Indian type (which is present in the Eastern region & the level of Hb F is 7-10%).

N.B: if the Hb A_2 is high → Sickle Cell - β-Thalassemia Disease.

➢ Indication of Blood Transfusion:

1] Crises (Hemolytic, Sequestration, Aplastic, but not Vaso-occlusive).
2] Hb < 6 g/dL.
3] Priapism.
4] CNS Crisis.
5] Renal Papillary Necrosis.
6] Acute Chest Syndrome.
7] Anesthesia & Surgery.

➢ Management:

1) Pirazetam: not useful.

2) Hydroxurea (antimetabolite):
- Action: ↑ *Hb F* → not used in patient with high Hb F.
- May cause Bone Marrow Suppression.
- Indications:
  a- Patient with low Hb F.
  b- if > 6 crises/year.
  c- Crisis e.g.

N.B: Bone Marrow Transplantation is not effective because Mortality Rate (10-15%) is higher than that of the disease itself.
N.B: The combination between Hb SS & α-Thalassemia is thought to be less severe than pure Hb SS disease because microcytosis, *resulting from α*-Thalassemia, allows better passage in the microcirculation.

- **G6PD Deficiency:**
  - X-linked (i.e. females are carriers)
  - 30% of the population are carriers.
  - Types: (both of them are present here)

  1) African (Favism): ingestion of fava beans, or certain drugs (such as aspirin, Antimalarial [e.g. chloroquine & primaquine], & those containing sulpha) → severe hemolytic anemia.
  2) Asian: spontaneous Hemolysis (may not be affected by fava beans).

- **Spherocytosis:**
  - *Autosomal dominant*.
  - Causing hemolytic anemia (acute or chronic) due to deformed shape of RBCs.
  - Clinical Features: may present antenatally with hemolytic anemia (whether acute or chronic & splenomegaly).
  - Treatment: Splenectomy.

- **Elliptocytosis:**
  - *Autosomal dominant*.
  - Benign.
  - Hemolytic anemia with splenomegaly.

- **Ovalocytosis:**

➲ **Hypoplastic or Aplastic Anemia:**

- Present with low Hb or Pancytopenia.

1) Congenital:

a- Pure Red Cell Hypoplasia (also called Diamond-Blackfan anemia):

- present at infancy.
- RBCs are selectively affected.
- might respond to steroids.

b- Fanconi Anemia:

- present at 4-5 years of age.
- Pancytopenia.
- Clinical Features: thin, short stature & other congenital anomalies including cardiac anomalies, skin pigmentation, renal anomalies.
- need Bone Marrow Transplantation.

2) Acquired:

a- Primary:

- Idiopathic.
- Majority of Aplastic Anemias are of this type.
- need Steroids or Androgens → if not resolve in 6 months → Bone Marrow Transplantation.

b- Secondary:

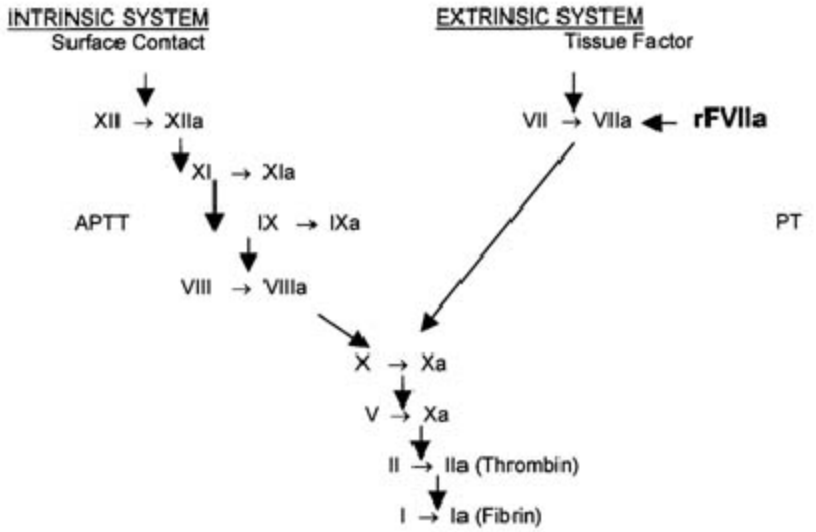
- e.g. infection with Hepatitis A virus or Parvovirus B19.

➢ Treatment:

- Mostly Bone Marrow Transplantation.
- If it is secondary, treat the cause.

The child with bruises and bleeding

1. Introduction:



- History:

  - Bruise onset:
    - Sudden (Acute)
    - From Infancy (Chronic, congenital, inheritant)
  - History of pallor, jaundice or bleeding
  - History of fever
  - History of bleeding tendency
  - Family History
  - History of drugs (Interfering with platelet function or coagulation cascade, e.g. Aspirin, NSAID).

- Physical Examination:

  Do a head to toe examination, observe the distribution of bruises, because certain conditions appear in specific sites. Check if it is purpura, bruise or petechiae.
  Examine for hepatomegaly, splenomegaly and pallor.

- Lab Investigations:

  - CBC (Hemoglobin, WBC, Platelets Count)
  - Blood Film
  - Bleeding Time, To role out platelet problem

- PT, Prothrombin Time: Extrinsic coagulation cascade
- PTT, partial thromboplastin time: Intrinsic coagulation cascade
- Factor Assay.

2. Platelets Problem:

Basics:

Platelets form in bone marrow from megakaryocytes. It is the first line in hemostasis, it releases factors after injury occurring that participate in vasoconstriction and clotting. The platelets form the plug which seals the most injuries, especially, minor ones. Platelet count is between 150- 250 X 10^3/mm^3, and its life span range from 7-10 days.

Platelets problems can be categorized into congenital and acquired and each subdivided into functional (Thrombasthenia), or Count (Thrombocytopenia)

- Congenital: these diseases are rare conditions;
  - Count: such as megakaryocytic thrombocytopenia (Autosomal Recessive)
  - Function: Glanzmann Thrombasthenia (Autosomal Recessive)

- Acquired:
  - Count: Thrombocytopenia
  - Function: e.g from drugs, there is prolongation of bleeding time, but platelet count is normal. This indicate doing platelet function test.

Thrombocytopenia:

- ITP (Idiopathic Thrombocytopenia)
- Secondary thrombocytopenia: Induced from different etiologies, e.g, infiltrative diseases, drugs, malignancy.

ITP:

Idiopathic or immune thrombocytopenia can be acute (mainly children), or chronic (Adults).

The acute ITP is common in 2-5 years old, but can occur at any age. It is preceded by upper respiratory tract infection which results in antibody formation Ig G that Coates the platelets. This ends in platelets destruction in the spleen. Anti platelets Antibody test found in 80 % of those children.

- ***Clinical Picture****:* ITP presents as bruises all over the body. There is no splenomegaly, hepatomegaly, nor lymphadenopathy. Anemia appears later, when patient bleed. So, other than bruises patient looks healthy and normal.

- ***Diagnosis****:* Bone marrow aspiration shows large (Giant) megakaryocytes.

- ***Management:***

It is a self limiting condition in 1-2 weeks, in most cases. But management of patients depends on platelets count;

- More than 25X 10^3 observe the patient for 1-2 weeks and see if the count increase or not, if it did not increase, start the treatment.
- Less than 25X 10^3 start the treatment immediately. Start the treatment with steroids, prednisolone 1-2 mg/Kg/day for 2-3 weeks with tapering over one week. So, after duration of steroid treatment, about one month, check the response. If there is no response, start I.V immunoglobulins.

If the condition persists for 6 months - 1 year, it is considered Chronic ITP. 90% by 6 months recover, less than 5- 10% persist into chronic ITP. Splenectomy may be indicated for conditions persisting 4-5 years.

So, the prognosis is excellent, but there is exacerbation and remission.

3. Henoch-Schonlein Purpura:

It is a vasculitis. It occurs in 5-7 years old children. It is preceded by Strept infection 3-4 weeks, by developing sub-conjunctivitis then forming antibodies attacking the vessels.

- ***Clinical Picture:***
  - Arthritis
  - Renal Involvement
  - Abdominal Pain
  - CNS
  - Rash below the waist, upper parts of body are spared

- ***Management:***

It is a self limiting condition. Only supportive treatment are given; analgesics and antibiotics for strept infection. Steroids are given, if there is involvement of kidney.

4. Coagulation Factors:

There are 13 factors responsible for coagulation, extrinsic and intrinsic cascades. They form the secondary line of hemostasis.

Coagulation factors

Coagulation factors and related substances	
Number and/or name	Function
I (fibrinogen)	Forms clot (fibrin)
II (prothrombin)	Its active form (IIa) activates I, V, VII, XIII, protein C, platelets
Tissue factor	Co-factor of VIIa (formerly known as factor III)
Calcium	Required for coagulation factors to bind to phospholipid (formerly known as factor IV)
V (proaccelerin, labile factor)	Co-factor of X with which it forms the prothrombinase complex
VI	Unassigned – old name of Factor Va

VII (stable factor)	Activates IX, X
VIII (antihemophilic factor)	Co-factor of IX with which it forms the tenase complex
IX (Christmas factor)	Activates X: forms tenase complex with factor VIII
X (Stuart-Prower factor)	Activates II: froms prothrombinase complex with factor V
XI (plasma thromboplastin antecedent)	Activates XII, IX and prekallikrein
XII (Hageman factor)	Activates prekallikrein and fibrinolysis
XIII (fibrin-stabilizing factor)	Crosslinks fibrin
von Willebrand factor	Binds to VIII, mediates platelet adhesion
prekallikrein	Activates XII and prekallikrein; cleaves HMWK
high molecular weight kininogen (HMWK)	Supports reciprocal activation of XII, XI, and prekallikrein
fibronectin	Mediates cell adhesion
antithrombin III	Inhibits IIa, Xa, and other proteases;
heparin cofactor II	Inhibits IIa, cofactor for heparin and dermatan sulfate ("minor antithrombin")
protein C	Inactivates Va and VIIIa
protein S	Cofactor for activated protein C (APC, inactive when bound to C4b-binding protein)
protein Z	Mediates thrombin adhesion to phospholipids and stimulates degradation of factor X by ZPI
Protein Z-related protease inhibitor (ZPI)	Degrades factors X (in presence of protein Z) and XI (independently)
plasminogen	Converts to plasmin, lyses fibrin and other proteins
alpha 2-antiplasmin	Inhibits plasmin
tissue plasminogen activator (tPA)	Activates plasminogen
urokinase	Activates plasminogen
plasminogen activator inhibitor-1 (PAI1)	Inactivates tPA & urokinase (endothelial PAI)
plasminogen activator inhibitor-2 (PAI2)	Inactivates tPA & urokinase (placental PAI)
cancer procoagulant	Pathological factor X activator linked to thrombosis in cancer

Hemophilia:

Hemophilia which is X-linked disease is the most common disease of this category, the other factors deficiency are rare. The incidence of hemophilia is 1/10,000 or 1/20,000. There are 3 types;

1. ***Hemophilia A***: 80-85% deficiency of factor VIII (anti-hemophilic factor), X-linked.
2. ***Hemophilia B*** (Christmas disease): 5-15% deficiency of factor IX (Christmas Factor), X-linked.
3. ***Hemophilia C***: <5% (rare deficiency of factor XI, Autosomal recessive.

Clinically all the types with same presentation, there is prolong PTT. To differentiate do factor assy.

Clinical Picture:

- Neonatal; appears after circumcision.
- If diagnosis was missed in early year of life, it appears in child after start walking at the end of his 1st year as Bruises from minor trauma or fall downs.
  Hemarthrosis is the commonest presentation, mainly in Knee, Elbow and Ankle. It appears as swollen, tender, hot, painful and difficult to move joint. The accumulated blood irritates the synovial membrane, eventually leads to erode the cartilage and as end result, organization in the joint and ankylosis, and atrophy of adjacent muscles.
  Management consist mainly of factor replacement, by increasing factor to >50 % at least.
- N.B/ do not manipulate the joint surgically, because it'll induce infections.
- Rash below the waist, upper parts of body are spared
- GIT, hematemesis, melena
- CNS bleeding

Generally, bleeding from any site of body can occur. The major inducer of bleeding is accident and trauma; even minor ones can lead to death.

- ***Diagnosis:*** PTT increases, Factor assay shows the deficient factor. Also antenatal diagnosis can diagnose the disease in-utero.

- ***Management:***

  - Medical:

    Factor replacement is the main treatment. There are many types of replacements;

    - Whole blood, for emergency cases only
    - Fresh frozen plasma, for emergency cases only
    - Cryoprecipitate
    - Pure Factor replacement (VIII, IX); carries less complication of transfusions.

    Minor bleeding (e.g., tooth extraction, simple hemarthrosis) requires factor increasing >= 50%.

    Major bleeding (e.g., CNS, major surgeries) requires increasing factors 100%.

    Factor VIII , 1 unit, increases factor plasma into 2% /Kg. Half life is 8- 12 hour , so must be given twice daily.

    Factor IX, 1 unit, increases factor plasma into 1% / Kg. Half life is 24 hour.

    5- 10% of patients develop inhibitors, so to manage either increase the dose or use steroids.

  - Genetic counseling and Education; teaching parents to take care of their children. Be cautiously from traumas, even minor ones.

- ***Complications:***
  - Chronic synovial arthropathy, it is now with proper treatment and prophylaxis is much less.
  - Infections related to transmitted disease by blood products transfusions. It is now less than before, due to check up done since 1990.
  - Psychological disorders

- Von-Willebrand Disease:

It is an autosomal dominant disease, with deficiency of VWF, Von Willebrand Factor. This factor is responsible in carrying & stabilizing of factor VIII and adhesive link between platelet and blood vessels. As so the deficiency leads into platelet dysfunction (Ristocetin dysfunction), and VIII deficiency.

- ***Clinical Picture:***
  - Mild to moderate bleeding
  - Mild to moderate hemarthrosis
  - Mucous membrane bleeding

- ***Diagnosis:*** Laboratory finding is characteristic, prolong bleeding time and PTT.

- ***Management***: Factor replacement and platelet transfusion.

Child cancer

Leukemia in children

- **Incidence:**

  White: $4.2 / 10^5$

  Black: $2.4 / 10^5$

- **Sex:** Male more than females

- **Age:** 2 – 10 years, but It can affect any age.

  The 2nd commonest cause of death in children between 2 – 10 (after accidents & poisoning).

  Leukemia represents 2/3 of all child cancers. (Commonest malignancy in children)

  It is the malignancy of bone marrow, commonly from WBC.

  Acute more than 95% , chronic 2-3%

  ALL 80 – 85%

  ANLL 15 – 20% Acute nonlymphocytic leukemia

► **N.B.** in children acute leukemia is more common than chronic unlike in adult

Also in children it is mostly of lymphoid type and that is why the prognosis is better than in adult leukemia which is mostly of myeloid type

- **Clinical manifestation:**

  Triad of **pallor** (anemia), **fever**, **bleeding** (thrombocytopenia), bone pain (due to infiltrations), weight loss, anorexia, lymphadenopathy, hepatosplenomegaly.

  So, leukemia is a disseminating disease.

- **Testicular leukemia:**

  Painless swelling

  Unilateral or bilateral

  - **Diagnosis:** biopsy only show blast cells (sheets of blast cells)
  - **Treatment:** with chemotherapy and radiotherapy.

- **CNS:**

1. Increase in ICP leads to vomiting, visual disturbance and headache.
2. Focal neurological manifestation (depend on the site of leukemic cells)

- **Diagnosis: work up of leukemia**
  - CBC: Low Hb, low platelets and high WBCs.
  - Blast cells
  - BMA (to investigate more)
  - CXR to find out the extent of the caner.
  - CSF
- **Morphological class of ALL**
  - L1 80 – 85 % small homogenous cells, little cytoplasm (nuclear / cytoplasm ratio is high)
  - L2 more (cytoplasm)
  - L3 more cytoplasm with granules

- **Cytochemical analysis of leukemia:**

	ALL	ANLL
TdT (terminal deoxy transferase)	+	-
PAS (periodic acid shiff)	+	-
Sudan black	-	+
Peroxidase	-	+
Esterase	-	+

- **Immunological class of ALL:**
  - Non B , non T : 80 – 85% (best prognosis and the commonest)
  - Early pre B or pro B
  - T –ALL: 10 – 15% bad prognosis
  - B- ALL: <5% (worst prognosis)
  - C- ALL (+): 80% (Good prognosis)
  - C-ALL (-) / null: 20% (bad prognosis)
- **Differential diagnosis of leukemia**
  - Infections (e.g. infectious mononucleosis)
  - Hematological (e.g. aplastic anemia, ITP)
  - Connective tissue disorders
  - Infiltrations

- **Good prognostic factors of ALL:**
  - No serious infections
  - White race
  - Age more than 2 and less than 10
  - Female
  - WBC less than 20.00 / cmm

- No CNS
- No mediastinal mass
- No testicular infiltration
- No gross organomegaly
- Normal chromosomes
- Non – B, non – T
- Normal platelets
- Adequate treatment
- L1

➢ **Management:**

a. Supportive:

- Isolation
- Infections
- Blood products
- Nutrition

b. specific:

- anti-neoplastic drugs
- BMT

➲ We assume that there is one kg of malignant cells in the circulation, so we use the best drugs

1. **Aim of induction (2 – 6 weeks)**
   - To kill 99.9% of malignant cells
   - To achieve remissions :
     - Clinical: disappearance of all signs and symptoms attributed to leukemia
     - Hematological: normal CBC and bone marrow cells less than 5%

2. **consolidation**
   - VP – 16
   - VM – 26
   - methotrexate
   - cyclophosphamide

   Aim to:
   1. prevent relapse
   2. kill any remaining cell (occult cells)

3. **CNC prophylaxis:** from the beginning (because if not used → relapse)

4. Maintenance

- 6MP : 50 – 75 mg/m2/day
- methotrexate 25
- cure: is disease symptom free and survival for 5 years
- prognosis: cure rate Is 70 – 80% with good prognostic factors
- cure rate is less than 40% with bad prognostic factors

➢ **Treatment of ANLL:**

- induction: A7D3 FVP-16
- CNS prophylaxis, IT MAH
- Maintenance: ARA – C, daunomycin
- Cure rate: in the best center 50%
- They usually end by BMT

➢ **Long term complications of leukemia:**

1. Growth failure
2. Endocrine failure
3. Neuropsychiatric

N.B. nowadays these complication become less common because decrease use of radiotherapy

4. secondary malignancy

Non-Hodgkin lymphoma

- **Incidence:** 7.4 / million
- **Sex:** males more than females
- **Etiology:**
  - Viral: EBV
  - Chromosomal
  - Immunodeficiency
- **Clinical presentation:**
- **Primary site:**
  - GIT most common
  - Jaw mass (burkits lymphoma)
  - Mediastinal

➲ **Systemic: NHL is a systemic disease from the start**

  - CNS
  - Testes
  - Renal
  - Anorexia
  - Anemia
  - Weight loss

- **Histological and immunological class of NHL IN CHILD:**
  - Lymphoblastic: T
  - Undifferentiated: B (most common)
  - Large cell type
- **Management:**

1. **Supportive**:
   - Nutrition
   - Blood products
   - Treatment of Infection
   - Treatment of Tumor lysis syndrome (TLS): increase K,P, URIC ACID which lead to RENAL FAILURE
   - Psychological
2. **Specific:**
   - Chemotherapy
   - Cure rate: excluding stage 4 the cure rate is more than 80%

Hodgkin lymphoma

- Incidence: 5 / million
- Sex: males more than females
- Age: 2 peaks late childhood

➢ **Clinical presentation:**

Cervical lymphadenopathy more than 90% (discrete, rubbery and painless)
Mediastinal mass
Abdomen involvement
N.B. HL is slowly growing tumor (late metastasis) and usually not involve BM, CNS, testes

➢ **Classification:**

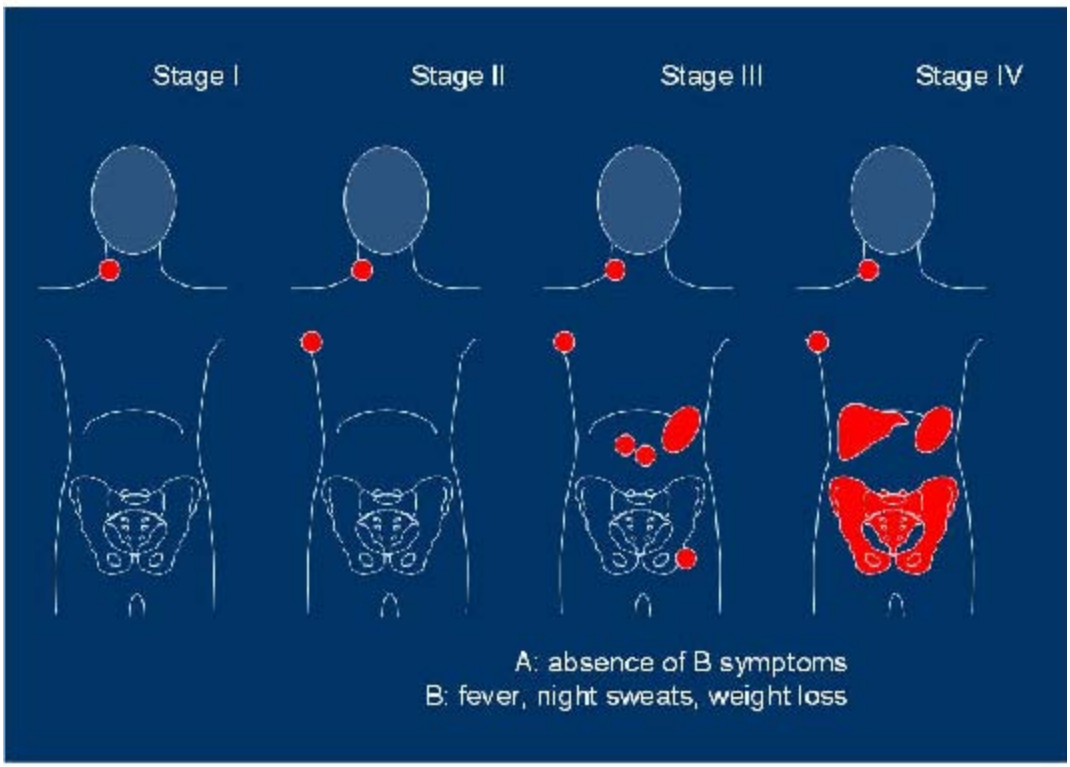
- Lymphocytic predominant (best prognosis)
- Nodular sclerosis
- Mixed cellularity
- Lymphocytic depletion (worst prognosis)

➢ **Diagnosis:**

BM biopsy (pathologic hallmark of HD is Reed-sternberg cells)

➢ **Treatment;**

Chemotherapy: 2 weeks treatment, 2 weeks rest for 6 months
ABVD: Adriamycin, bleomycin, vinblastine



- **Prognostic factors:**

1. **stage**: is the most important factor
   Stage 1 and 2 have cure rate of more than 90%
   Stage 3 have cure rate of more than 70%
   Stage 4 have cure rate of less than 50% (stage 4 –B has worse prognosis than 4 – A)
2. histopathology
3. age
4. erythrocyte

Solid tumors

Brain tumors :(2nd commonest malignancy after leukemia followed by lymphoma)

- **Incidence:** 24 per million
- **Sex:** males more than females (apart from medulloblastoma)
- **Etiology:** unknown
- **Predisposing factors:**
  - Radiotherapy
  - Neurofibromatosis
  - neurocutaneous syndromes (e.g. tuberous sclerosis)
- **Classes of brain tumors:**

1. **supra tentorial** (most common in adults):
   - craniopharyngioma
   - meningioma
   - astrocytoma
2. **infra tentorial** (most common in children):
   - astrocytoma
   - medulloblastoma
   - ependymoma
   - Brainstem glioma

- **Clinical manifestation:**

N.B. the most important thing is early diagnosis of the tumor because the only definite treatment is surgical resection.

➲ **Increase ICP causes:**
   - Headache
   - Visual problems
   - Macrocephaly
   - Focal neurological deficits

➲ **On x – ray:** widening of the sutures (to day we depend on CT and MRI).

- **Treatment:**
  - Surgery (mainstay treatment)
  - Radiotherapy
  - Chemotherapy

Wilm's tumor (nephroblastoma)

- **Origin:** Arise from metanephrons
- **Incidence:**
  Blacks: 7.8 per million
  White: 7.5 per million
- **Sex:** males equal females
- **Age:** mostly within the first five years of life and peak in the 1 – 2 years
- **Etiology:** unknown

- **Predisposing factors:**
  - Associated with some congenital anomalies like; hypospadias, undescended testis, aniridia and hemihypertrophy of the limbs
  - Familial

- **Clinical presentation: the most benign tumor**
  - Abdominal mass 100%
  - Abdominal pain 27%
  - Hematuria 16.5%
  - Hypertension 11%
  - Ascitis 5.5
  - Metastasis <5% (most common site is the lung)

- **Pathology of wilm's tumor:**

o Favorable (well differentiated) 90%
o Unfavorable (not well differentiated) 10%

- **Diagnosis works up:**

CBC, urine, stool, AXR (mass not cross the mid line, no calcification, distortion of the calyces), US, BMA, tissue biopsy, LFT, RFT, CT, bone scan.
All these work up to find if there is metastasis

Staging:	**Cure rate***
Stage 1 Tumor is limited to the kidney and is completely excised	more than 90%
Stage 2 Tumor extends beyond the kidney but is completely excised	more than 90%
Stage 3 Unresectable primary tumor, Lymph node metastasis	
Stage 4 hematogenous metastases (lung, liver, bone, or brain),	(worst prognosis)
Stage 5 (bilateral) an attempt should be made to stage each side according to the above criteria	

***N.B.cure rate is** (2 years survival without the evidence of the disease)

- **Treatment:**

Combination of:

- Surgery: nephrectomy
- Chemotherapy: VCR, ACT-D, ADRIAMYCIN
- RADIOTHERAPY: only for stage 3, 4

Neuroblastoma:

- **Origin:** neural crest cells
- **Incidence:** white 9.6 per million
  Blacks 7.7 per million

In situ 1 / 200 – 1 / 1000 (incidence after autopsy)

This means that there is tendency to spontaneous regression

- **Age:** less than 5 years
- **Sex:** ***females*** more than males
- **Etiology;** unknown
- **Clinical presentation:** depend on the primary site:
  - Abdominal mass more than 50%
  - Metastasis (commonest site to the orbit and skull bones)
  - Systemic early weight loss, anorexia, diarrhea
  - Hypertension (during intrauterine life due to increase catecholamines)
  - Eye proptosis
  - Nasopharyngeal obstruction
  - Opsomyoclonus (nystagmus + myoclonus)

N.B. this tumor is a fast growing tumor usually cross the midline and early metastasis

(at time of presentation it is usually stage 4).

➲ **Stage 4 s:**

Patient with neuroblastoma present less than 1 year with skin, BM, or liver involvement.

High tendency for spontaneous regression (excellent prognosis)

- **Biochemical finding in neuroblastoma:**
  - High VMA, HVA
  - High ferritin
  - High cystathionuria
  - High alpha fetoprotein (AFP)
  - High cranioembrionic antigen (CEA)
  - High neuro specific enorate (NSE)

- **Diagnosis works up:**

AXR (cross the mid line, calcification, the kidney is push down)

Diagnosis by biopsy

- **Pathology of neuroblastoma:**
  - Neuroblastoma (associated with metastasis)
  - Ganglioneuroblastoma
  - Ganglioneuroma (not associated with metastasis)

- **Differential diagnosis of neuroblastoma:**
  - osteomyelitis
  - autoimmune; RA
  - SCA
  - Leukemia
  - Wilms' tumor
  - Ewing's sarcoma

- **Metastasis:**
  - Bone (most common especially orbit)
  - BM
  - LN
  - Liver

- **Treatment:**

Surgical resection is the primary treatment

Stage 1, 2 90% cures (if totally resected)

Stage 3 60 – 70% cures (if totally resected)

Stage 4 less than 30% (very poor prognosis)

Chemotherapy:

- Vincristine
- Cyclophosphamide
- Adriamycin
- Cisplatinum
- Vm 26 / VP 16

➢ **Prognostic factor:**

- Stage (most important factor)
- Age
- Histopathology

Glomerulonephritis

NOTE; this subject was taught to us as TUTORIAL by Dr. Chisti. So I did my best to make it as comprehensive as I can & I wrote wvery single word the doctor said. Please accept my prior apology for any weak sentences

- **Definition:**
  - Pathologically: it is an inflammation of glomeruli
  - Clinically: nephritis is a triad of hematuria, hypertension and azotemia

  - Usually, these patient present with smoggy urine, dark urine, decrease amount of urine, headache as symptom of HTN, edema as symptom of azotemia is GN.
  - Hematuria (may be gross or microscopic) doesn't have to be gross, WHY? b/c there are certain type of GNs which will give microscopic hematuria & cast

- **Q/ what do you need to confirm the diagnosis of GN?**

UA: specifically, RBC cast.
N.B; when you see RBC cast in urine, it's GN until proven otherwise.

- **CASE 1;**
  9 year old male with h/o coca-cola colored urine for 2 days, presented to ER complaining of headache & facial puffiness since the morning.

- **What important questions & things you'll ask in the history for this patient? (N.B; focus only in GNs as differentials, b/c even hemolysis & HF could be a differential.)**
  - h/o of URTI ? Possibility of PSGN. It's the commonest & easy to diagnose
    N.B; strep is not the only organism that causes GN. As a start PSGN will be called post INFECTIOUS GN . the other organisms are: strep, pneumococcus, staph, meningococcus, Ebstein-Bar virus, adenovirus…etc
  - Urine output? b/c you want to know what's going on , how badly kidney function is affected.
  - Any member of the family has same symptoms?
    b/c hereditary nephropathy e.g. ALPORT syndrome (Deafness, vision [keratoconus, lentoconus stigmatism], all MATERNAL uncles [ẏ ẋ ẏ] has problem, X-linked)

- Any skin rash? b/c Henoch-Schönlein purpura (HSP) may have something like IgA GN, they also have Hx of URTI. The rash starts maculopapular then progress to purpuric rash, usually over buttocks.
- Any hemoptysis? b/c of vasculitis e.g. Goodpasture disease
- Joint problem? b/c Connective Tissue disease e.g. SLE, PAN, Wegener , mixed C/T disorders.
  N.B; children with Wegener syndrome will have nasal polyp, recurrent sinusitis & granulomatous inflammation
- Hx of bloody diarrhea? b/c of hemolytic Uremic syndrome (HUS). Classically it's not GN, b/c it's a microangiopathy & hemolytic uremia caused by thrombosis of renal vessels
- Recurrent? b/c IgA GN is recurrent

N.B; dark urine could be UTI, but if there's no urinary symptoms then it's not

Regarding this case, this patient has h/o URTI 4 weeks ago, decrease in urination for 2 days, no family hx, no rash, no hemoptysis, no joint pain, no bloody diarrhea, no recurrence & urinary symptoms.

- **What physical exam you will do to strengthen your history?**

the examination In this patient is as following :

- Vital sign; BP (KEY) 150/95, b/c HTN
- Dark urine & edema is GN
- Wt & Ht are within 50TH percentile (so this is acute)
- CNS; intact
- Fundoscopy; NL
- Chest; bilateral crepitation
- Abdomen; ascites
- Extremities; pitting edema

N.B; we can add to the differentials a disease not usually classified as GN which is Focal Segmental Glomerulosclerosis (FSGS). FSGS can present like GN with cast in urine, gross hematuria. FSGS itself is a pathologic entity that can be present with IgA, ALPORT, and PSGN..etc

What lab do we want?

- Urine analysis: look for
  RBC
  Protein
  RBC cast

N.B; hematuria never worries us, RBC cast & proteinuria do worry us. b/c hematuria is benign, with exam Repetition it will disappear.

N.B; even in nephritis there's an entity called Nephrotic Nephritic syndrome. It's GN with high proteinuria.

- RFT; if there's abnormality, it'll strengthen the diagnosis

- Serology; for strep: 1- ASO
- N.B; because both sore throat & skin infection can cause GN and ASO ↑ *only with sore throat so we should also do:*
  2- Anti-Hyaluronidase
  3- Anti-DNase B
  N.B. more often positive following skin infections

- C3, C4 (complement); do them both

- IgA; IgA level really doesn't help
  If +ve → ↑*suspicion*
  If –ve → *does not R/O IgA*
  It's found ↑ *in 30% of patients* of IgA nephropathy
- ANA (antinuclear antibody);
  It's a good test
  It's a screening for all C/T diseases

- Biopsy; it's indicated in the followings:
  1- any patient with RPGN
  2- if complement does not return to NL within 6-8 weeks
  3- if RFT is severe at presentation
  4- if complement is low & serology is –ve
  5- if patient's ANA is +ve THEN AdsDNA is +ve

➲ ***BASIC TEST:***

- CBC; Hb, platelet (HUS)
- RFT

These 2 should be done to all patients

- Electrolyte
- ANA, C3, C4
- ASO, Anti-Dinase B, Anti Hyaluronidase titer

➲ ***ADVANCED:***

- Anti ds-DNA
- ANCA (antineutrophil cytoplasmic antibody)
- Anti GBN antibodies
- Serum IgA level
- Renal biopsy

N.B; for all GNs, there's no magic treatment. All GNs mostly heal by themselves

Steroid is not used to all GNs

MANAGEMENT;

Patient in ER with HTN, edema & affected kidney function, what will you do?

1- admit the patient (ADMISSION)
2- put patient in SALT & WATER RESTRICTION, why?
b/c patient is already overload & edematous. So basically, he's in acute renal failure
3- manage HTN;
Think why HTN is there, why? It's either salt mediated OR Renin associated.
So, 1st line of ttt for BOTH fluid overload & HTN is DIURETIC (lasix). If BP gets better, fair enough. If doesn't, 2nd line of ttt is usually Ca-channel blocker. Why not ACEI, although renin share responsibility in causing HTN?
b/c ACEI ↓ *perfusion pressure through glomeruli In kidney.* All we need to ttt GN is time, good blood flow, good oxygenation & good nutrition. So if we ↓ *perfusion pressure* → ↓ *blood flow* → ↓*oxygenation …etc. That's why no need* for ACEI now.

N.B; in PSGN, HTN is actually short-lived (7-10 days). In Some cases, HTN prolongs up to 3-4 months. Now, after acute phase, you are allowed to use ACEI. So, regarding HTN:

- in acute phase → *diuretic* + *Ca*-channel blocker
- in chronic phase → *ACEI*

4- Then you do restriction of intake & output, and then decide how much fluid you are going to give. If patient make any good urine, you really don't need to be worried about fluid restriction. If not, you will go to same steps as acute renal failure, insensible urine output replacement.

5- If there's electrolyte abnormalities, you deal with them

- **A million dollar question: does this child need Antibiotics?**
  Basically, patient with PSGN doesn't need AB b/c the disease is an immunologic response to an infection that already over. What we do is we take a throat culture, if +ve (carrier or acute infection) → *give AB, if* –ve → *no need to AB. So, AB has* no role in GN.

  Now lets say that it's been 3 days since ttt, BP is in good control, patient is doing well, not febrile, making good urine, creatinine is NL, ASO +ve, Anti Dinase B & Anti Hyaluronidase are –ve. So most probably it comes from throat. The C3 is ↓.
- **Do you have the diagnosis of PSGN?**
  NO, this still could be MPGN. If ASO titer is done for a group of people, > 50% of them will be +ve b/c strep infection is very common, and once infected ASO become +ve.
  ↓ *C3 seen in* → *MPGN (1/3 has ↓ complement)*
  → *PSGN*
  → *SLE*
- **So, what proves PSGN?**
  You have to repeat complement in 6-8 weeks, & it has to return to NL. Before that we only write GN.

Family education is important regarding hematuria, that hematuria lasts for 12-18 months to disappear. This important b/c when the patient gets sick & goes to GP, the GP once see microscopic hematuria, he'll think of UTI & will prescribe AB that's not necessary for the patient

- **1% of patient with PSGN develops RPGN. How rapid?**
  Within 4-6 w to 6 m, RFT changes from NL to ESRD

ANCA (antinuclear cytoplasmic antibody):
ANCA is 2 types P-ANCA & C-ANCA
If strep serology is –ve, complement is low, ANA is +ve, then we'll do ANCA. Then I'll do biopsy & follow P-ANCA & C-ANCA for the disease activity.
If ANCA is +ve → *it's Wegner granulomatosis or PAN*

CASE 2:

11-year-old girl c/o;

- Headache
- Facial puffiness in the morning
- Irritability & excessive anger for the last week
- +ve frequency, urgency & dysuria
- Joint pain
- Oral ulcers
- Rash appear on face when exposed to sun

➲ ***Diagnosis is SLE***

Here the basic work-up is the same but in advanced work-up we'll have ANA, Anti ds-DNA in ER. For strep serology, we'll do ASO titer ONLY. After that 24-h urine to decide how much is proteinuria

➲ ***Stages of lupus GN:***

0- NL
1- Mild proliferative GN
2- Mesangio-proliferative GN
3- Focal proliferative GN
4- Diffuse proliferative GN
5- MPGN

(1-2 ttt with steroid, 3-5 ttt with cyclophosphamide)

CASE 3:

7-year-old boy has h/o microscopic hematuria & proteinuria detected incidentally on school physical exam.

- Has no complaint on presentation
- No urinary symptoms nor change in urine color
- No trauma
- No joint pain or oral ulcers
- No blurred vision
- No rashes
- No hair loss
- He has h/o URTI 3w ago
- He has h/o gross hematuria 3m ago (this isn't asymptomatic PSGN)
- No family history

GN is either IgA, ALPORT or Thin Basement Membrane disease. The later is usually benign, but in minority of patient it can even progress to end stage.

In this case, the differentials will be;
IgA, Hereditary nephropathy, …etc

The patient is not even hypertensive

We'll do the basic work-up, & we'll add 24-h urine collection for protein. Also to get GFR & serology

The patient is completely clear of symptoms, only 1g protein in urine.

➲ ***So, WHAT WILL YOU DO?***
A biopsy.

➲ ***Advanced:***
When you get a patient like this who's completely asymptomatic, you look for 4 things before biopsy:
1- growth
2- proteinuria
3- kidney function
4- HTN
If 2 or more present, then I'll do biopsy. Otherwise, no need for it.

➲ ***MANAGEMENT:***
All these parameters are NL in this child except for proteinuria. The diagnosis is IgA GN.
This patient will be followed every 3-4 months for these 4 parameters.

What can u do for a patient with symptomatic IgA?
Steroid, immunosuppression & fish oil
N.B; these only retard or slow the progression of the disease

The wheezy child

- Most of you will see wheezy child but that doesn' t mean asthma
- 25% of babies <5yrs may have wheezing during auscultation.

✓ **Wheezing:** is an audible continuous musical sound heard during auscultation of chest
- It may have low or high pitch, single or multiple, inspiratory or expiratory which indicates severity of obstruction, intrathoracic or extrathoracic may indicate the cause, it could be monophonic or polyphonic.

✓ **Differential diagnosis of wheezing:**
1. bronchial asthma : the top of the list
2. bronchiolitis
3. foreign body aspiration
4. aspiration pneumonia, GERD
5. cystic fibrosis
6. congenital anomalies
7. bronchopulmonary dysplasia
8. heart failure

Note: not all wheezy child means asthma, it depends on presentation.

A. Bronchial asthma:

✓ **Definition:** acute onset of paroxysmal (goes, come, night or day) spasmodic attack (reversible or irreversible) of cough, dyspnea and wheezing.
- It does not mean all pt. has dyspnea or wheezing.

✓ **Pathophysiology:** at cellular level
1. Air way inflammation → air way edema (2ry to inflammation)
2. Mucus plug formation
3. Smooth muscle contraction.

This is why the patients differ in respond to medication or not. Because some pt. have airway edema, other have mucus plug just needs suctioning of mucus or coughing, some have bronchospasm which response to bronchodilators not to anti-inflammatory.

- ✓ **Prevalence:**
  - It occurs at any age.
  - 30% of have symptoms by 1st yr of age
  - 8-10% by 4-5 yrs
  - Most of patients as they grow up they become cleanout of symptoms by the age of 6-7 yrs.
  - 5% will be continuous to adult and have severed type of asthma.

- ✓ **Triggering factors:**

When present the pt. keep in mind triggering factors

1. allergens: which pt aware about it
2. exercise
3. viral infection
4. some types of medication
5. Some tumors.
6. Smoking.

- ✓ **Transient wheezing:**

Patients with chronic emphysema, pulmonary dysplasia or trauma 2ry to intubation for long period -in general- they have diminished lung size

At age of 5 yrs most of them will be have normal pulmonary function, and the symptoms will improve by the end of 6-7 yrs of age.
However some patients have wheezing from beginning and still continue to have, these patients usually have risk factors e.g. parent's smokers, elevated IgE on immunological study, strong family history of bronchial asthma and allergy.

In spite of improving of medication of asthma, the prevalence of asthma increase for all years, mortality rate also increase esp. less than 1 year.

What does it mean?

Reasons:

1. Improper assessment of the pt.
2. Local hospital treatment, because not all medication that provided are available in the markets.
3. Compliance in spite of education.
4. Exposure of triggering factors.

✓ **Risk factors of fatal asthma:**

If u don't present these factors in the exam will be trouble or proven otherwise

1. previous attacks of sever asthma
2. Past Hx. Of respiratory failure
3. Hx. Of ICU admission
4. multiple medication
5. Seizure due to hypoxia.

If we have predisposing factors, casual factors and contributing factors all these initiate of immune response in the body , there is air way inflammation , with persisting contributing factors lead to premorbid air way, if not inhibited at this stage you will end up with air way remodeling which is air way limitation " very difficult to treat" you will have what is called compensating hyperventilation with normocapnia at one stage, and if left without management the end result will be sever hyperventilation with hypercapnia.
N.B. if there is hyperventilation you should expect hyperresonance on percussion.

In histology: air way shows muscle tightness with small diameter with long untreated asthma

✓ **Signs:**

General appearance:
Cyanosis, if u sees pt. have cyanosis 1st gives him (to start with oxygen then Ventolin.

Chest: deformity
Pectus excavatum: depression lower border of sternum.

✓ **Diagnosis of asthma:**

1. Coughing
2. SOB.
3. Wheezing
4. Chest tightness
5. Sputum production
6. Pulmonary function test
7. Response on bronchodilators or steroid

Some times history is the only way to diagnose and differentiate asthma from cystic fibrosis.

✓ **Pattern of symptoms:**

Perennial, seasonal, frequency, duration, diurnal variation

✓ **Precipitating factors:**

1. Viral inf." Most of time"
2. environmental
3. cold
4. drug exposure
5. occupation

✓ **Diagnosis:**

Response of medication

Pulmonary function test:

Force vital capacity "volume" in one sec. (FVC1) is decreased

Chest x-ray:

Not routinely requested, it request to role out bronchopneumonia or complication pneumothorax or pneumomediastinum

CBC

Sputum examination

Eosinophils count

Elevated IgE

Esophageal pH: to exclude GERD

ABG :(MCQ)

Initial norm capnia then hypercapnia

✓ **Chronic asthma:**

	Mild intermittent	Mild persistence	Moderate persistence	sever
Day Sx	=<2/Wk	>2/wk	>2/wk	continuous
Night Sx	=<2/month	>2/month	>1/wk	Frequent
PFT	FEV1 or PEV =>80% predicted PEV variability <20%	FEV1 or PEV >80% predicted PEV variability 20-30%	FEV1 or PEV >60% to <80% predicted PEV variability >30%	FEV1 or PEV =<60% predicted PEV variability >30%

U should know the severity of disease, in order to treat the patient and to determine when he needs ICU admission.

- ✓ **Indication of ICU admission:**
  1. Family Hx. Of respiratory failure
  2. Previous Hx. Of failure to improvement to regular medication
  3. Cardiopulmonary arrest
  4. ABG: metabolic acidosis 2ry to respiratory hypoxia or other causes
  5. PFT: not improving with medication.

- ✓ **Treatment: 6 elements**

Unfortunately most of us just assets and monitor the severity without educate the parents about risk and aggravating factors.

In general:

1. Oxygen 2. Anticholinergic
3. Steroid 4. Theophylline: no role in chronic asthma
5. Intubate and gastric tube

- ✓ **Treatment according to severity:**

Mild intermittent	PRN medication
Mild persistence	PRN medication+ low dose anti-inflammatory
Moderate persistence	PRN medication+ anti-inflammatory optimize the dose + relax?
Severe	Short term medication

Side effect of ventolin" salbutamol":

Tachycardia, hypokalemia

Side effect of anticholinergic" ipratropium":

Much less cardiac side effect comparing to other medication

Steroid:

Give improvement of PFT after 4 h and significant improvement after 6h

Oxygen:

Don't forget some people think the oxygen suppress respiratory center, this is untrue, and it is true in COPD.

Rehydration:

Most of pt. is dehydrated; it is due to tachypnea and sweating
U should not over hydrated the pt. which end up with pulmonary edema
Some times may ends up with SIADH whish is manifested with hyponatremia.

Intubating is not routinely indicated.

B. Bronchiolitis:

2nd of big list of causes of wheezing
It is acute infectious disease of lower respiratory tract that primarily in young
Part of differential diagnosis of wheezy child before 2 yrs
2% of pt. are admitted to hospital esp. those of less than 6 month, that' s mean it is more benign than asthma
Mechanical ventilation requires 2% out of 2% that admitted to hospital.
Mortality rate 1-2% of all pt. not as asthma

✓ **Common agents:**

RSV
Para influenza type1, 2, 3.
Influenza type B
Mycoplasma "atypical bacteria"

N.B. Pt. present to ER has hx. Of apnea and cough u should include bronchiolitis

✓ **Risk factors:**

The disease correlate very well of

1. 1st infection
2. post conceptional age < 24 wks
3. Premature or gestational age less than 24wks.
4. less than 6mon: more than other age gps

Tachypnea and hypoxic are best picture, but not correlate with degree of illness

✓ **TREATMENT**

Supportive therapy
Fluid, oxygen, well monitoring

Is bronchodilator effective?
Bronchodilators have not much role in bronchiolitis except if you suspect asthma
Corticosteroid: does not has a role at all as opposite as asthma" evidence support"

Antiviral "ribavirin" which requested to pt. with CHD, bronchopulmonary dysplasia ,cystic fibrosis, multiple congenital anomalies and less than 6d old.

C. Foreign body aspiration:

Sudden onset of cough some times cyanosis during chocking episode
Most of times are young children.
N.B. chest x-ray shows hyperinflation on affected side because air comes in but no out.

D. GERD

Apnea and bradycardia
May have stridor, loss of appetite, pneumonitis
Usually 4-5 yrs age of children

E. cystic fibrosis

- Autosomal recessive
- Patient has repeated chest infection and sticky mucus secretion.

F. tracheomalacia

E. bronchomalacia

VACCINE & VACCINATION

- **OBJECTIVES**
  - **Eradication of diseases (e.g. small pox)**
  - **Prevention of disease in individual or groups**

- **Types of Immunoprophylaxis:**
  - **Active immunization**
  - **Passive immunization**

I-ACTIVE VACCINATION

- **Definition.**

  Administration of all or part of a micro-organism or a modified product of that micro-organism (e.g. a toxoid, a purified antigen or an antigen produced by genetic engineering) to evoke an immunologic response mimicking that of the natural infection but without any risk to the recipient.

- **Effectiveness.**

  Assessed by the evidence of protection against the natural disease.

  E.g. by decrease the incidence of the disease

  Or by measuring the level of antibodies in the blood

- **Type of active immunization:**
  - *Live attenuated.*
  - *Killed (inactive or subunit)*

a. Live & Attenuated:

1. Induce active infection (b/c you introduce the whole organism)
2. Elicit wide range of immunologic response
3. Limit use in immune-compromised individuals and pregnancy
4. Most viral vaccine
   - MMR
   - Measles
   - Mumps
   - Rubella
   - BCG (TB is not viral infection)
   - OPV
   - Typhoid
   - Yellow Fever

b. Killed (Inactivated or Subunit)

1. Incapable of replication
2. Must contain sufficient antigenic mass
3. Require periodic administration of booster doses
4. May not elicit desired immunological response
5. Side effect is more severe should it occurs
6. Does not effect immuno-compromised host
7. Most bacterial and some viral vaccines:

- DTP
- H. Influenza
- Cholera
- Pertussis
- Meningococcal
- Rabies
- Hepatitis
- Pneumococcal
- Typhoid

✓ IMMUNIZATION ANTIGENS

1. Active immunization antigens
   - Single antigen (pneumo., tetanus)
   - Complex antigen (live viruses or killed bacteria)
2. Suspending fluid
   - Simple (water or saline)
   - Complex (protein to keep the organism alive)
3. Preservatives stabilizers and antibiotics
4. Adjuvant
   - Increase immunogenicity & prolong the stimulatory effect

✓ SITE & ROUTE OF IMMUNIZATION

1. Oral vaccines

- Breast feeding
- Regurgitation & vomiting

2. Parenteral Vaccines

The recommended route depends on the result of prior clinical use that demonstrated maximum safety and efficacy.

➲ **SC injection:**

- The easiest way to give the vaccine
- Anterolateral aspect of the thigh or the upper arm by inserting the needle in a pinched up for of skin

➲ **ID injection:**

- Most painful route (b/c the it will separate the dermis from the epidermis where the nerve roots are present)
- Injections generally are given on the volar surface of the forearm

➲ **IM injection:**

- Children < 1 year the anterolateral aspect of the thigh provides the largest muscle and the preferred sit
- Older children the deltoid muscle is preferred
- *Ordinary the upper, outer aspect of the buttocks should not be used for active immunization because the gluteal region is covered by a significant layer of subcutaneous fat and because of the possibility of damaging the sciatic nerve*

***Complication of IM injection*:**

- Muscle contracture
- Nerve injury
- Abscesses Bacterial & Sterile
- Skin pigmentation
- Hemorrhage, cellulites and tissue necrosis
- Broken needles and local atrophy

✓ SCHEDULING IMMUNIZATIONS

Factors that determine immunization schedule:

- Epidemiology of disease at specific age
- Presence of residual maternal antibodies
- Achievement of uniform & regular response
- Age specific response and availability

Immunization schedule in KSA

Age	Immunization
Birth	BCG & Hepatitis*
2 months	DTP, OPV, H. Infl. & Hepatitis
4 months	DTP, OPV & H. Infl.
6 months	DTP, OPV, H. Infl. & Hepatitis
12 month	MMR
18 month	DTP & OPV Booster

*b/c TB and hepatitis infection could acquire from the mother so the vaccine is given at birth

➲ **Is vaccination mandatory in Saudi Arabia?**

By law, it is not but they don' t give the birth certificate unless the child is vaccinated

✓ **SIMULTANEOUS ADMINISTRATION OF MULTIPLE VACCINES**

- Most vaccines can be safely and effectively administered simultaneously
- Immune response to one vaccine do not interfere with those of other vaccine
- Simultaneous administration of vaccines has sero-conversion rate & rate of side effects similar to vaccine s administered at separate times
- ***Recommended to :***
  - **Doubtful return for further immunization**
  - **Foreign travel**
- ***A lapse in the immunization schedule dose not require reinstitution of the entire series***

✓ **VACCINATION OF PRETERM INFANTS**

- Vaccine doses should not reduced
- Hepatitis vaccine should be given when the infant weight *is > 2 kg*
- If infants still hospitalized at 60 days and weight at least 1500 gm should be given DPT, HIB and IPV (not OPV).
- Live virus vaccine should never be given during hospitalization

VACCINE & VACCINATION

➲ **BCG:**

Bacilli Chalmette Guerin Vaccine

- Live attenuated vaccine (Mycobacterium Bovis)
- Mechanism of Protection is largely unknown but cellular immunity has been shown
  - ***Effectiveness:***
    - TB infection 50%
    - TB meningitis 64%
    - Disseminated TB 78%
    - Death 71%
  - ***Contraindications:***
    - Altered immune status
    - Burns or extensive skin disease
    - Positive tuberculin test
    - With measles or mumps vaccine
    - Pregnancy

➲ **Diphtheria Toxoid**

- Prepared by formaldehyde detoxification of diphtheria toxin
- Mechanism of protection by formation of neutralizing antibodies (antitoxin)
  - ***Effectiveness:***
    - Very effective for at least 10 years
  - ***Contraindication:***
    - Anaphylactic reaction
    - With DTP there should be no contraindication to other components

➲ **Pertussis Vaccine:**

- Inactivated whole Bordetella Pertussis.
- Mechanism of protection:
    - Induce multiple antibodies to B. Pertussis antigen
  - ***Effectiveness:***
    - No precise estimate but highly effective vaccine
  - ***Contraindications:***
    - Anaphylactic reaction to previous dose
    - Encephalopathy within 7 days of a pervious vaccine
    - Acute febrile illness
    - Unstable or progressive neurological illness

- ***Precautions:***
  - Hyperpyrexia with temperature > 40.5^{o}C
  - Collapse state within 48 hours
  - Persistent inconsolable crying for more than 24 hours
  - Convulsions within 3 days
- ***Non-contraindications:***
  - Stable neurological conditions
  - Family history of convulsions
  - Family history of SIDS
  - Family history of adverse event following the vaccine

➲ **Tetanus Toxoid:**

- Prepared by formaldehyde detoxification of tetanus toxoid
- Mechanism of protection:
  - Production of neutralizing antibodies (antitoxins)
- ***Effectiveness:***
  - Very effective for at least 10 years.
- ***Contraindications:***
  - Severe systemic reaction to a previous dose
  - Development of major local reaction or fever

➲ **Oral Polio vaccine (OPV):**

- Mixture of three types of live attenuated poliovirus
- Mechanism of protection:
  - Local secretory IgA at GIT so preventing implantation and multiplication of wild virus
  - Humoral antibody (IgM & IgG)
- ***Effectiveness:***
  - After multiple administrations more than 90% of vaccines will be protected.
- ***Contraindications:***
  - Patients with altered immunity and house hold contacts
  - Infants with family history of proven or suspected primary immunodeficiency disorders
  - Anaphylactic reactions

➲ **Inactivated Polio Vaccine (IPV):**

- Contains mixture of all three types of polioviruses which is killed
- Mechanism of protection:
  - Induction of neutralizing antibodies in the serum
  - Promote immune system to response to exposure to wild virus
- o ***Effectiveness:***
  - 100% efficacy
- o ***Contraindications:***
  - History of anaphylactic reaction.

➲ **Hepatitis B Vaccine:**

- Purified particles of the surface antigen of the virus (HBsAg)
- Mechanism of action:
  - Induce antibodies (Anti-HBsAg)
  - Immune memory against Hepatitis B virus
- o ***Efficacy: (course of 3 IM doses)***
  - 90% in adults
  - 95% in infants
- o ***Contraindications:***
  - Hypersensitivity to any component of the vaccine

➲ **Hemophilus influenzae type B:**

- Purified capsular polysaccharide of HIB
- Mechanism of protection by:
  - Inducing antibodies against HIB
  - Reducing the asymptomatic HIB nasopharyngeal colonization
- o ***Efficacy:***
  - Very effective after a single dose in children over 18 months of age
  - Multiple doses are needed in infants
- o ***Contraindications***
  - In patients with history of severe allergic reaction to the vaccine

➲ **Measles Vaccine:**

- Live attenuated virus
- Mechanism of protection:
  - Induced IgG & secretory IgA in nasal secretions
  - Stimulation of cell mediated immunity

- ***Effectiveness:***
  - Similar to that of natural infection
- ***Contraindications:***
  - Individuals with altered immunity
  - History of anaphylactic reaction
  - Pregnancy

➲ **Mumps Vaccine:**

(Mumps could be very serious in males b/c it can cause orchitis)

- Live attenuated virus
- Mechanism of protection:
  - Neutralizing antibodies are induced in serum
  - Cell mediated immunity
- ***Effectiveness:***
  - Clinical protection in 90-95% of vaccinees
- ***Contraindications:***
  - Individuals with altered immunity
  - History of anaphylactic reaction
  - Pregnancy

➲ **Rubella Vaccine:**

(Rubella is more worth in females b/c it can lead to congenital anomalies to the fetus)

- Live attenuated virus
- Mechanism of Protection:
  - Induction of neutralizing antibodies in serum
  - Production of IgA antibodies in nasopharynx
  - Simulation of cell-mediated immune response
- ***Effectiveness:***
  - Similar to that of natural infection
- ***Contraindications:***
  - Altered immune status
  - Pregnancy
  - Anaphylactic reaction
  - Administration of immunoglobulin or other blood product 2 weeks before vaccination

CONTRAINDICATIONS & PRECAUTIONS

- ***Misconception concerning vaccine contraindications***
  1. Mild acute illness with low grade fever
  2. Mild reaction to previous DPT vaccine i.e. soreness, redness, swelling at the vaccine site or temp. < 40.5° C
  3. Current anti-microbial therapy
  4. Prematurity or low birth weight

- ***REAL CONTRAINDICATIONS & PRECAUTIONS***
  1. Encephalopathy within 7 days
  2. Persistent severe inconsolable crying for 3 hours (this is a sign of Encephalopathy)
  3. Collapse or shock like state within 48 hours
  4. Fever of 40.5°C or more
  5. Immediate allergic reaction to vaccine (severe or anaphylactic in type)
  6. Immunodeficiency status (Congenital acquired or therapeutic) for live vaccine

  Note: most of contraindications are occur after receiving the vaccination (no.1,2,3,5) and if the child will receive the vaccination for the first time there is no cut point contraindication (only 4 &6)

II-PASSIVE IMMUNIZATION

Administration of preformed antibody to a recipient

- ***Indications:***
  a. When person is deficient in synthesis of antibodies as result of congenital or acquired B-lymphocyte factors
  b. When person susceptible to the disease is exposed or has a high likelihood of exposure to the infection
  c. Therapeutically, when a disease is already present

- ***Types:***
  a. IG (Immune Globulin) not specific.
  b. Specific Immune Globulin (e.g. zoster, hepatitis)
  c. Human Plasma
  d. Antibodies of animal origin

Meningitis

- Hippocrates was aware of the intracranial complications of otitis, and unequivocal descriptions of meningitis are found as easily as the 17th century.
- Visseux first described the syndrome of meningitis as being a purpuric rash in 1805.
- By the end of the 19th century, Neisseria meningitides, Diplococcus pneumonia, and Haemophilus influenzae had all been isolated at autopsy from CSF of patients with meningitis.
- 25,000 cases of meningitis are seen each year in the United States.
- Meningitis implies primary involvement of the meninges, whereas encephalitis indicates brain parenchymal involvement.
- Meningoencephalitis is the involvement of both the meninges and brain parenchyma.

Bacterial Meningitis:

- It is one of the most potentially serious infections in infants and older children.
- It is associated with high rate of acute complications and risk of chronic morbidity.
- It should be included in the differential diagnosis of altered mental status such as lethargy or irritability, or evidence of other neurologic dysfunction in febrile infants.

Causative Organisms of Bacterial Meningitis (Percentage of Cases by Age)

Organism	Neonates (≤1 month)	Children (1 month–15 years)	Adults (15–60 years)	Adults (>60 years)
Haemophilus influenzae	4	52	5	15
Neisseria meningitidis	1	27	30	10
Streptococcus pneumoniae	3	15	40	5
Gram-negative bacilli	50	2	5	15
Streptococci	35–40*	2	5	3
Staphylococci	5	1	10	2
Listeria species	2	1	5	15

**Nearly all isolates are group B streptococci.*

Agents Causing Meningitis According to Patient Age

▶ Neonates	*Streptococcus agalactiae*, in particular type III
	Escherichia coli and other Gram-negative organisms (*Proteus mirabilis, Klebsiella-Enterobacter* species, *Pseudomonas aeruginosa, Citrobacter diversus, Salmonella species*)
	Listeria monocytogenes
	Staphylococcus epidermidis
	Staphylococcus aureus
	Streptococcus pneumoniae
▶ Childhood to early adulthood	*Neisseria meningitidis*
	S pneumoniae
	S aureus
▶ Midadulthood	*S pneumoniae*
	S aureus
▶ Old age	*S pneumoniae*
	S aureus
	L monocytogenes
	Gram-negatives

✓ **Epidemiology:**

➲ **Major risk factors:**

- The lack of immunity to specific pathogens associated with young age.
- Recent colonization with pathogenic bacteria.
- Close contact (e.g. household, day care centers, schools, military barracks) with individuals having invasive disease.
- Crowding, poverty.
- Black race, male sex.
- Absence of breast-feeding for infants 2-5 months of age.

✓ **Mode of transmission:**

Person to person contact through respiratory tract secretions or droplets.

➲ **The risk of meningitis is increased among:**

- Infants and young children with occult bacteremia.
- Defect in specific host defense e.g.
- Altered immunoglobulin production in response to encapsulated pathogens.
- Defects of the complement system (C5-C8) have been associated with recurrent meningococcal infection.
- Defects of the properdin system have been associated with a significant risk of lethal meningococcal disease.
- Splenic dysfunction is associated with an increased risk of encapsulated organisms.
- T-lymphocyte defects are associated with an increased risk of L. monocytogenes infection.
- Congenital or acquired CSF leak across a mucocutaneous barrier is associated with an increased risk of pneumococcal meningitis.
- Lumbosacral dermal sinus is associated with staphylococcal and gram-negative enteric bacterial meningitis.
- Penetrating cranial trauma and CSF shunt infection is associated with staphylococci (especially coagulase negative species).

Agents Causing Meningitis According to Route of Acquisition

Condition	Probable Organism(s)
▶ Sinusitis or otitis	*Streptococcus pneumoniae, Haemophilus influenzae,* anaerobic streptococci, *Bacteroides, Staphylococcus aureus*
▶ Penetrating head trauma	*S aureus*
▶ Shunt infections	*Staphylococcus epidermidis*
▶ Complications of neurosurgery	Gram-negative bacteria (*Klebsiella pneumonia, Acinetobacter calcoaceticus, Escherichia coli*)

✓ **Pathology:**

Meningeal exudates of varying thickness may be distributed around the cerebral veins, venous sinuses, and convexity of the brain, and cerebellum and in the sulci, sylvian fissures, basal cisterns and spinal cord.

- Ventriculitis with bacteria and inflammatory cells in ventricular fluid may be present, as may subdural effusion and, rarely, empyema.
- Vascular and parenchymal cerebral changes characterized by polymorphonuclear infiltrates extending to the subintimal region of the small arteries and veins, vasculitis, thrombosis of small cortical veins, occlusion of major venous sinuses, necrotizing arteritis producing subarachnoid hemorrhage, and, rarely, cerebral cortical necrosis . Cerebral infarction is a frequent sequela of vascular occlusion from inflammation, vasospasm, and thrombosis.
- Inflammation of the spinal nerves and roots produces meningeal signs, and inflammation of the cranial nerves produces cranial neuropathies of optic, oculomotor, facial, and auditory nerves.
- Increased ICP also produces oculomotor nerve palsy due to the presence of temporal lobe compression of the nerve during tentorial (uncal) herniation. Abducens nerve palsy may be a non localizing sign of raised ICP (b/c of its long course).

➲ **Increased ICP due to:**

- Cell death (cytotoxic cerebral edema).
- Cytokine-induced capillary vascular permeability (vasogenic cerebral edema).
- Increased hydrostatic pressure (interstitial cerebral edema) after obstructed reabsorption of CSF in the arachnoid villus or obstruction of the fluid from the ventricles.
- SIADH may produce excessive water retention, increasing the risk of raised ICP.
- Hypotonicity of brain extracellular spaces may cause cytotoxic edema after cell swelling and lysis.

➲ **Hydrocephalus is an uncommon acute complication of meningitis occurring *after the neonatal period*.**

- It most often takes the form of a communicating hydrocephalus due to adhesive thickening of the arachnoids villi around the cisterns of the base of the brain. Thus, there is interference with the normal resorption of CSF.

- Obstructive hydrocephalus develops after fibrosis and gliosis of the aqueduct of sylvius or the foramina of Magendie and Luschka.

➲ **Raised CSF protein levels are due in part to increased vascular permeability of the blood – brain barrier and the loss of albumin- rich fluid from the capillaries and veins traversing the subdural space.**

- Continued transudation may result in subdural effusions.

➲ **Hypoglycorrhachia (reduced CSF glucose levels) is due to decreased glucose transport by the cerebral tissue.**

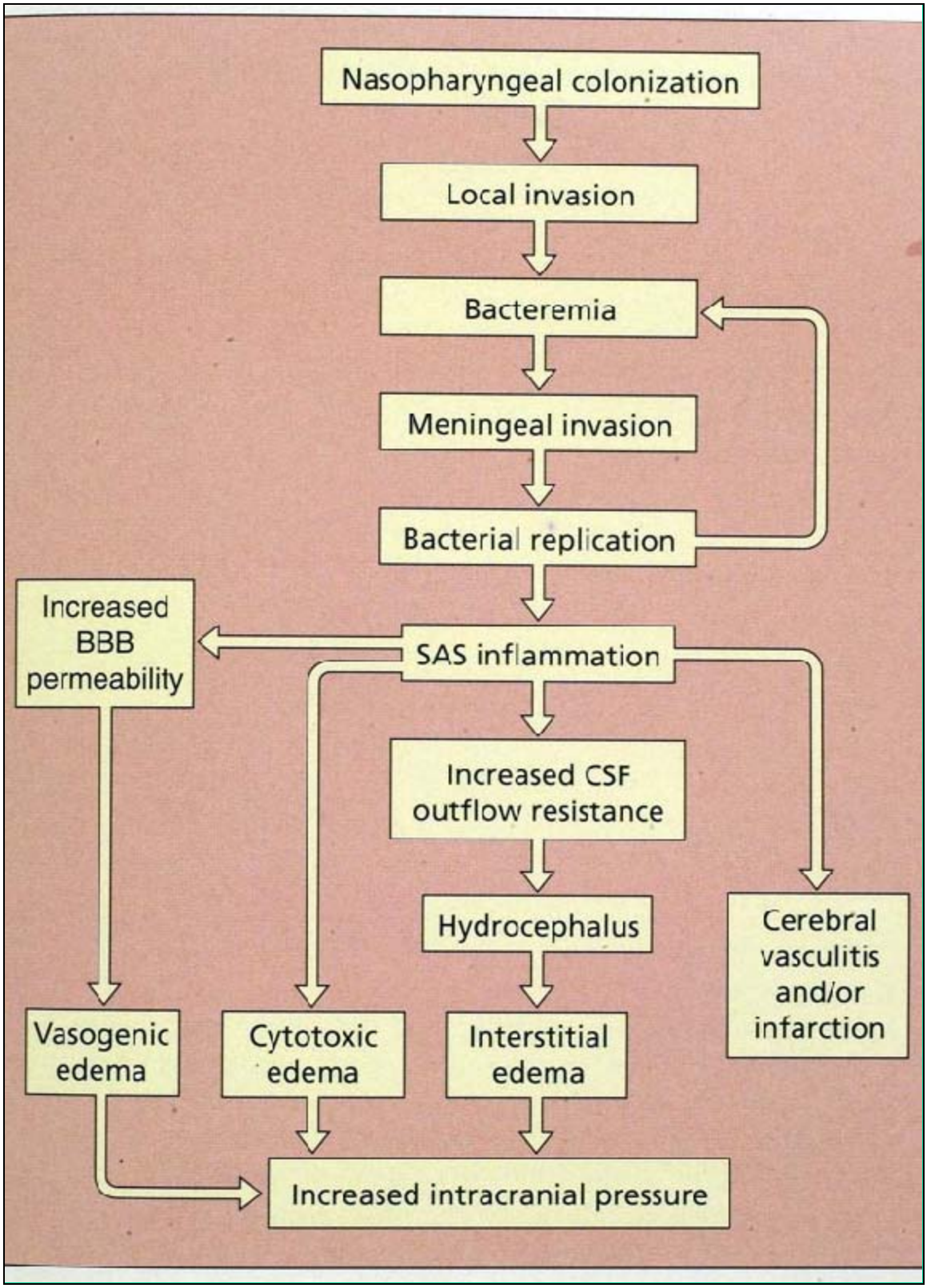
➲ **Damage to the cerebral cortex may be due to:**

- The focal or diffuse effects of vascular occlusion (infarction, necrosis, and lactic acidosis).
- Hypoxia.
- Bacterial invasion (cerebritis).
- Toxic encephalopathy (bacterial toxins).
- Raised ICP.
- Ventriculitis.
- Transudation (subdural effusions).

These pathologic factors result in clinical manifestations of impaired consciousness, seizures, hydrocephalus, cranial nerve deficits, motor and sensory deficits, and later psychomotor retardation.

✓ **Pathogenesis:**

- Most frequently meningitis is the consequence of hematogenous dissemination of organisms from sites of infection outside the central nervous system.
- Less frequently, meningitis may be caused by the direct spread of agents from infected pericranial structures, such as sinuses, middle ear, or mastoid, or by entry of organisms through congenital or acquired defects in the skull or spinal column. It is especially important to search for such defects in patients with recurrent meningitis.
- Inflammation within the subarachnoid space is often accompanied by encephalitis involving the underlying cortex as well as ventriculitis, at times with secondary hydrocephalus.
- Spread of inflammation into superficial areas of brain may result in thrombosis of superficial cerebral vessels.



✓ **Clinical presentation:**

Bacterial meningitis typically presents in one of three ways:

1. Most meningitis is preceded by 3-5 days of insidiously progressive symptoms of fever, malaise, irritability, or vomiting.
2. In a smaller number of cases, meningitis develops over 1-2 days.

3. In a minority, bacterial meningitis begins fulminantly (sudden onset with rapidly progressive manifestations of shock, purpura, DIC and reduced levels of consciousness frequently resulting in death within 24 hr.

➲ **Typical symptoms are:**

- Fever (90-95%), headache, photophobia, and change in mental status.
- Anorexia and poor feeding, symptoms of upper respiratory tract infection, myalgias, arthralgia, tachycardia, hypotension, and petechiae, purpura, or an erythematous macular rash.

✓ **Physical examination:**

- Fever.
- Tachycardia.
- Nuchal rigidity.
- Altered mental status.
- Papilledema.
- Cutaneous rashes: petechiae or purpura suggestive of meningococcemia.
- Pulmonary consolidation may be present in S. pneumoniae meningitis.
- Cardiac murmurs, suggestive of endocarditis.

✓ **Tests of meningeal irritation:**

- Brudzinski's sign: involves spontaneous flexion of the hips and knees when the neck is passively flexed (more sensitive).
- Kernig's sign: is resistance to passive extension of the leg at the knee.
- Ask the patient either to kiss a knee or to touch the forehead to the knees.

➲ **Signs of meningeal irritation are often absent in 5 groups of patients:**

1. Neonates (bulging fontanel, apneic spells, high pitched cry, atypical seizures, and changes in HR).
2. Immunosuppressed patients.
3. Patients with meningitis related to neurosurgical procedures.
4. The elderly.
5. Alcoholics.

- **Signs of increased ICP:**
  - Headache.
  - Emesis.
  - Bulging fontanel or diastasis of the sutures.
  - Oculomotor or abducens nerve paralysis.
  - Hypertension with bradycardia.
  - Apnea or hyperventilation.
  - Decorticate or decerebrate posturing.
  - Stupor.
  - Coma.
  - Signs of herniation.
  - Papilledema.
- **Focal neurological signs due to:**
  - Vascular occlusion.
  - Focal inflammation.
  - These include cranial neuropathies of ocular, oculomotor, abducens, facial, and auditory nerves.
- **Seizures due to:**
  - Cerebritis.
  - Infarction.
  - Or electrolytes disturbances.

✓ **Laboratory diagnosis of meningitis:**

Typical CSF Findings in Bacterial Meningitis

Opening pressure	Usually elevated
Fluid	Turbid
Cells	>100/mm^3; often >1000 cells/mm^2
Cell type	Polymorphonuclear leukocytes
Protein	Elevated: usually >100
Glucose	Depressed: usually <50% of blood glucose
Gram's stain	Positive in 60% to 80% of cases

➲ **Contraindication for an immediate LP:**

- Evidence of increased ICP (other than a bulging fontanel), such as 3rd or 6th cranial nerve palsy with depressed level of consciousness, or hypertension and bradycardia with respiratory abnormalities.
- Severe cardiopulmonary compromise resuscitative measures for shock or in patients in whom positioning for LP would further compromise cardiopulmonary function.
- Infection of the skin overlying the site of the LP.
- Thrombocytopenia is a relative contraindication for immediate LP.

Note: if LP is delayed, immediate empirical therapy should be initiated.

✓ **Latex particle agglutination:**

- Test to detect bacterial antigen in the CSF.
- It is used in patients who were receiving antibiotics and their cultures were negative.

➲ **Blood cultures should be performed in all patients with suspected meningitis.**
It is positive in 80-90% of cases of childhood meningitis.

Type of infection	Predominant cells (mm3)	Glucose mg/dl	Stain for organisms	diagnosis
Bacterial meningitis	PMNs	Very low (0-10)	Gram stain	Culture, CIE, LA, LAL, CoA
TB meningitis	Monos	Low to very low (10-20)	Ziehl-Neilson	Culture
Viral meningitis	Monos	Normal	-	Culture
Fungal meningitis	Monos	Low (15-30)	Cryptococcus-Indian ink	Culture, various Ab & Ag tests
Parameningeal meningitis	Subacute & chronic →Monos (usual picture) Acute → PMNs (uncommon)	Normal	-	CT, MIR, Myelogram
Neoplastic meningitis	Monos	Low to normal (30-50)	-	Cytogenic studies

➲ **Focal infection of the CNS:**
- Brain abscess.
- Parameningeal abscess (subdural empyema, cranial and spinal epidural abscess).

➲ **Noninfectious illnesses:**
- Malignancy.
- Collagen vascular syndromes.
- Exposure to toxins.
- Acute viral meningoencephalitis: patient may appear less ill than those with bacterial meningitis.

➲ **Partially treated meningitis:**
- 25-50% of children being evaluated for bacterial meningitis are receiving oral antibiotics when their CSF is obtained.
- Frequently positive CSF Gram Stain results and ability to grow the bacteria may be reduced.
- The concentration of CSF glucose, and protein, and neutrophil profile are not substantially altered by pretreatment.

✓ **Treatment:**

➲ **Two requirements for the antimicrobial agents to reach the infected meninges:**

1. They must be bactericidal for the causative agent.
2. They must be able to penetrate the blood brain barrier.

- The initial (empiric) choice of therapy should be based on the antibiotic susceptibilities of S.pneumoniae, N. meningitides, and H. influenzae.
- 25-50% of strains of S.pneumoniae are currently resistant to penicillin and 5-10% of the isolates are resistant to cefotaxime and ceftriaxone.

♦ N.meningitides are sensitive to penicillin and cephalosporins. Rare resistant isolates have been reported.
♦ 30-40% of isolates of H. infuenzae type b produces B-lactamases and therefore are resistant to ampicillin. B-lactamase-producing strains are sensitive to the extended-spectrum cephalosporins.
♦ Empirical therapy to S.pneumoniae:
♦ Either of the third-generation cephalosporins, cefotaxime (200 mg/kg/24hr given every 6 hr)
♦ Combined with vancomycin (60mg/kg/24 hr, given every 6 hr).

- L.monocytogenes: ampicillin (200mg/kg/24 hr, givin every 6hr)+ ceftriaxone or cefotaxime or IV trimethoprim-sulfamethoxazole.
- Gram-negative bacterial meningitis: ceftazidime and an aminoglycosides.
- S.aureus: nafcillin, oxacillin, vancomycin.
- Anaerobic organisms such as Bacteroides fragilis: metronidazole.

Duration of antibiotic therapy:

- Uncomplicated S. pneumoniae: 10-14 days.
- Uncomplicated H. influenzae: 7-10 days.
- Uncomplicated N. meningitides: 5-7 days.
- If no pathogen identified, should continue ceftriaxone or cefotaxime for 7-10 days.

➲ Corticosteroids:

- Rapid killing of bacteria in the CSF effectively sterilizes the meningeal infection but releases toxic cell products after cell lysis (cell wall endotoxin) that precipitates the cytotoxic-mediated inflammatory response. The resultant edema formation and neutrophilic infiltration may produce additional neurologic injury with worsening of CNS signs and symptoms.
- IV dexamethasone, 0.15mg/kg/dose given every 6hr for 2 days, in the treatment of children older than 6 weeks with acute bacterial meningitis, especially for H. influenzae type b.

Advantage of corticosteroids:

- Limit production of inflammatory mediators.
- Less fever.
- Lower CSF protein and lactate level.
- Reduction in permanent auditory nerve damage, as manifested by sensorineural hearing loss.

✓ Complications of meningitis:

➲ Neurologic complications:

- Seizures.
- Increased ICP.
- Cranial nerve palsies.
- Stroke.
- Cerebral or cerebellar herniation.
- Transverse myelitis.
- Ataxia.
- Thrombosis of dural venous sinuses.
- Subdural effusions.

➲ **Subdural effusion:**
- 10-30% of patients with meningitis.
- Asymptomatic in 85-90% of patients.
- Common in infants.
- Symptoms include bulging fontanel, diastasis of sutures, enlarged head circumference, emesis, seizures, fever, and abnormal results of cranial transillumination.
- Dx: CT or MRI scanning of the brain.
- Rx: aspiration of the fluid through the open fontanel in the presence of symptoms of increased ICP or a depressed level of consciousness.

➲ **SIADAH:**
- 30-50% of patients with meningitis resulting in hyponatremia and reduced serum osmolality.
- It may exacerbate cerebral edema or independently produce hyponatremic seizures.
- Central diabetes insipidus may develop as a result of hypothalamic or pituitary dysfunction.

➲ **Fever:**
- It usually resolves within 5-7 days of onset of therapy.
- 10% of patient, a prolonged fever > 10 days is noted.
- Caused of prolonged fever:
    - Intercurrent viral infection.
    - Nosocomial or secondary bacterial infection.
    - Thrombophlebitis.
    - Drug reaction.

♦ Pericarditis or arthritis may result either from bacterial dissemination or from immune complex deposition.
♦ Thrombocytosis and eosinophilia.
♦ Anemia may be due to hemolysis or bone marrow suppression.
♦ DIC is associated with rapidly progressive pattern of presentation and is noted most commonly in patients with shock and purpura.

✓ **Prognosis:**
- Mortality rate after appropriate recognition prompt antibiotic therapy and supportive care after the neonatal period is 1-8%.
- Severe neurodevelopmental sequelae may occur in 10-20%.
- Neurobehavioral morbidity is 50%.

➲ **Poor prognosis in:**
- Infants younger than 6 months and those with more than 10,000,000 colony-forming units of bacteria/ml in their CSF.
- Seizures occurring more than 4 days in therapy.
- Coma or focal neurologic signs on presentation.

➲ **Neurologic sequelae:**
- Sensorineural hearing loss due to labyrinthitis following cochlear infection or due to direct inflammation of the auditory nerve.
- Mental retardation.
- Seizures.
- Delay in acquisition of language.
- Visual impairment.
- Behavioral problems.

➲ **Repeated episodes of meningitis are rare and have 3 patterns:**

➲ **Recrudescence:** reappearance of infection during therapy with appropriate antibiotics.

➲ **Relapse:** occurs between 3 days and 3 weeks after therapy and represents persistent bacterial infection in the CNS (subdural empyema, ventriculitis, cerebral abscess) or other site (mastoid, cranial osteomyelitis, or orbital infection)

➲ **Recurrence:** is a new episode of meningitis due to reinfection with the same bacterial species or another pyogenic pathogen.

✓ **Prevention:**
- Vaccination and antibiotic prophylaxis of susceptible at-risk contacts.
- An outbreak of meningitis within families is uncommon, although temporary nasal carriage occurs frequently with S.pnemoniae, N.meningitides, and H.influenzae.
- Prophylaxis is not usually an issue with close contacts of patients with S.pnemoniae meningitis, but in cases of meningitis due to N.meningitides or H.influenzae.
- As a rule chemoprophylaxis should be administered only to individuals who frequently eat and sleep in the same dwelling as the index case.

The child with convulsions

- 4-6 cases/1,000 children.
- The most common cause for referral to a pediatric neurology practice.
- The presence of a seizure disorder does not constitute a diagnosis but a symptom of an underlying CNS disorder that requires a thorough investigation and management plan.

✓ **Definitions:**

➲ **A seizure (convulsion):** is a paroxysmal involuntary disturbance of brain function that may manifest as an impairment or loss of consciousness, abnormal motor activity, behavioral abnormalities, sensory disturbances, or autonomic dysfunction. Some seizures are characterized by abnormal movements without loss or impairment of consciousness.

➲ **Epilepsy:** is recurrent seizures unrelated to fever or to an acute cerebral insult.

✓ **Evaluation:**

A) History:

- Define factors that may promote the convulsion.
- Detailed description of the seizure and the child postictal state e.g. type, duration, state of consciousness, aura, behavioral change, posture of the patient, cyanosis, vocalizations, loss of sphincter control, frequency, time of the day, and change of the type of the convulsion.
- Intellectual deterioration, and constitutional symptoms e.g. vomiting and failure to thrive.

➲ **Risk for epilepsy:**

- First convulsion in association with a viral illness a low grade fever.
- Seizures that occur during the early morning hours or with drowsiness, or during the initial phase of sleep.

- **Focal seizures:** it is characterized by motor or sensory symptoms and include:
  - Forceful turning of the head and eyes to one side.
  - Unilateral clonic movements beginning in the face or extremities.
  - Sensory disturbance e.g. paresthesias or pain localized to a specific area.
  - Cause is idiopathic in childhood.

- **Motor seizures:**
  - May be focal or generalized.
  - Tonic-clonic.
  - Tonic.
  - Myoclonic.
  - atonic

- **Tonic seizures:** are characterized by increased tone or rigidity.
- **Atonic seizures**: are characterized by flaccidity or by lack of movement during a convulsion.
- **Clonic seizures:** consist of rhythmic muscle contraction and relaxation.
- **Myoclonus:** is a shock like contractions of a muscle.
- **Aura**: most common aura in children consists of epigastric discomfort or pain and feeling of fear.

B) Examination:

- V/S.
- Head circumference and weight.
- Unusual facial features.
- Neurocutaneous stigmata e.g. vitiliginous lesions, adenoma sebaceum (Tuberous Sclerosis), shagreen patch, multiple café-au-lait spots, nevus flammeus, retinal phakoma.
- Localizing neurologic signs e.g
  - hemiparesis with hyper-reflexia.
  - downward-drifting extended arm with eyes closed suggest a contralateral hemispheric structural lesion.
  - a unilateral growth arrest of the thumbnail, hand, or extremity in a child with focal seizure disorder suggests a chronic condition e.g. porencephalic cyst, arteriovenous malformation, or cortical atrophy in the opposite hemisphere.

- Eye ground examination for papilledema, retinal hemorrhage, chorioretinitis, coloboma, and macular and retinal changes.
- Hyperventilation for 3-4 minutes.

✓ **Classification of seizures:**

- Reasons for seizure classification:
  - The seizure type may provide a clue to the cause of the seizure disorder.
  - Precise delineation of the seizure may allow a firm basis for making a prognosis.
  - The electroencephalogram (EEG) is a useful adjunct to the classification of epilepsy.

✓ **International classification of epileptic seizures:**

a) Partial seizures:
   1) Simple partial
      - motor
      - sensory
      - autonomic
      - psychic
   2) Complex partial
      - Simple partial, followed by impaired consciousness.
      - Consciousness impaired at onset.
   3) Partial seizures with secondary generalization.

b) Generalized seizures
   1) Absences: - Typical.
      - Atypical.
   2) Generalized tonic clonic.
   3) Tonic.
   4) Clonic.
   5) Myoclonic.
   6) Atonic.
   7) Infantile spasms.

C) Unclassified seizures.

➲ **Partial seizures:**

- ~ 40% of childhood seizures.

➢**Simple partial seizures (SPS):**

- Motor activity is the most common symptom of SPS.
- Movements are characterized by asynchronous clonic or tonic movements, and they tend to involve the face, neck, and extremities.
- Versive seizures consist of head turning and conjugate eye movements.
- *Automatisms do not occur.*
- Aura may occur e.g. chest discomfort and headache.
- Duration is 10-22 seconds.
- EEG may show spikes or sharp waves unilaterally or bilaterally, or a multifocal spike pattern.
- DD: tics.

➢**Complex partial seizures (CPS):**

It may begin with a simple partial seizure with or without an aura, followed by impaired consciousness, or, conversely, the onset of the CPS may coincide with an altered state of consciousness.

a) Impaired consciousness in the child is difficult to appreciate. There may be a brief blank stare overlooked by the parents.
The child is unable to communicate or to describe the periods of impaired consciousness in most cases.
The periods of altered consciousness may be brief and infrequent which may be seen by an experienced observer or an EEG.

b) Automatisms:

- Are common feature of CPS, 50-70%.
- it develops following the loss of consciousness and
- May persist into the postictal phase.
- In infants, it is characterized by alimentary automatism e.g. lip smacking, chewing, swallowing, and excessive salivation.
- In older children, it consists of semi purposeful, incoordinated, and unplanned gestural automatisms e.g picking and pulling at clothing or the bed sheets, rubbing or caressing objects, and walking or running in a nondirective, repetitive, and often fearful fashion.

c) Secondary generalization:

- During the spread of the ictal discharge throughout
- The hemisphere, a contralateral versive turning of the head, dystonic posturing, and tonic or clonic movements of the extremities and face including eye blinking.

- Duration: 1-2 minutes.
- EEG: interictal anterior temporal lobe sharp waves or focal spikes, and multifocal spikes ~ 20% of the patients with CPS have a normal routine interictal EEG.
- CT- scanning or MRI are most likely to identify an abnormality in the temporal lobe e.g. mesial temporal sclerosis, hamartoma, post encephalitic gliosis, subarachnoid cyst, infarction, A-V malformation, and slow growing glioma.

➲ **Benign partial epilepsy with Centro temporal spikes (BPEC):**

- A common type of partial epilepsy in childhood.
- Excellent prognosis.
- Age between 2 & 14 years, with peak age of onset 9-10 years.
- It occurs in normal children.
- There often a positive family history of epilepsy.
- The seizures are usually partial, and motor signs and somatosensory symptoms are ***confined to the face***.
- Oropharyngeal symptoms include tonic contractions and paresthesias of the tongue, unilateral numbness of the cheek, guttural noise, dysphagia and excessive salivation.
- Unilateral tonic clonic contractures of the lower face accompany the oropharyngeal symptoms, as do clonic movements or paresthesias of the ipsilateral extremities.
- Intact or impaired consciousness and it may proceed to secondary generalization.
- In *75% of patients occurs during sleep*.
- EEG: Centro temporal or rolandic spikes in a normal background.
- Carbamazepine is indicated only for patients with frequent seizures.

- **Generalized seizures:**
  - **Absence seizures:**
    - Typical absence (petit mal) seizures are characterized by a sudden cessation of motor activity or speech with a blank facial expression and flickering of the eyelids.
    - More prevalent in girls> 5 years old.
    - Never associated with aura.
    - No postictal state.
    - Duration: < 30 seconds.
    - No loss of body tone but the head may fall forward slightly.
    - Hyperventilation for 3-4 minutes produces a seizure.
    - EEG: 3/sec spike and generalized wave discharge.
  - **Rx: Ethosuximide or valproate.**

    Phenobarbital, phenytoin, and carbamazepine are not effective.

- **Juvenile myoclonic epilepsy:**
  - Onset 12-16 years.
  - Accounts for ~ 5% of the epilepsies.
  - Patients note frequent ***myoclonic jerks*** upon ***awakening,*** which makes hair-combing and tooth-brushing difficult.
  - A few years later, early morning generalized tonic-clonic seizures develop in association with the myoclonus.
  - EEG: 4-6/sec irregular spike and wave pattern, photoparoxysmal.
  - **Rx: valproate life long.**

- **Infantile spasms (IS) :**
  - Onset: 4 and 8 months.
  - Characterized by brief symmetric contractions of the neck, trunk, and extremities.
  - **Types:**

    a) Flexor spasms: occur in clusters or volleys and consist of sudden flexion of the neck, arms, and legs into the trunk.

    b) Extensor spasms: produce extension of the trunk and extremities, and are the least common form of IS.

    C) Mixed IS consisting of flexion in some volleys and extension in others, is the most common type of IS.

    - Duration: may persist for minutes.

- The spasms occur during sleep or arousal but a tendency to develop while the patient is drowsy or immediately upon awakening.
- EEG: hypsarrhythmia, disorganized background activity, with a chaotic high voltage, bilaterally asynchronous, slow wave activity.

➢**Classification:**

➲ **Symptomatic: 80-90%**

- Related to several prenatal, perinatal, and postnatal factors.
- Prenatal and perinatal factors include HIE with periventricular leukomalacia, congenital infections, inborn errors of metabolism, neurocutaneous syndromes, and cytoarchitectural abnormalities.
- Postnatal conditions: CNS infection, head trauma, and HIE.
- 80-90% risk of mental retardation.

➲ **Idiopathic : 10-20%**

- The child has uneventful pregnancy and birth history as well as normal developmental milestones prior to the onset of seizures. Normal neurological examination and neuroimaging study.
- Good prognosis.

➢**Rx: Intramuscular adrenocorticotropic hormone ACTH for 4-8 weeks. Valproate and clonazepam may be helpful.**

➲ **Febrile seizures: 3-4% of young children.**

- Onset between 6 month and 5 years of age in the context of fever, usually > 38.5ºC, and most often as the temperature rises or is at its peak. Implicitto the definition is an absence both of metabolic disarray and of nervous system infection.
- The seizures are usually grand mal, although they can be tonic, atonic, or clonic.
- Simple febrile seizures are single, non-focal, and last less than 15 minutes.
- Atypical febrile seizure: more than one seizure within 24hr, greater than 15 minutes, focal, and abnormal neurological examination.

- All febrile patients under 18 months of age with a first seizure require lumbar puncture and a metabolic screen.
- Risk factors for subsequent development of epilepsy include:
  - Antecedent abnormal neurologic or developmental status.
  - A family history of febrile seizures.
  - Complex febrile seizures.
- The presence of a single risk factor is associated with a < 2% chance of development of afebrile seizures.

➢**Prophylaxis for febrile seizures:**

- Medications proven to be effective prophylactically include phenobarbital, diazepam, and valproate.
Carbamazepine and phenytoin are not effective.
- Indication for prophylaxis are:
  - Frequent seizures.
  - Recurrent life threatening seizures (status epilepticus).

✓ **Diagnosis of seizures:**

- History.
- Physical examination.
- Minimum work-up for a first afebrile seizure in an otherwise healthy child includes:
  - fasting glucose
  - Calcium
  - Magnesium
  - Serum electrolyte levels.
  - EEG

- Prolonged EEG monitoring with simultaneous closed-circuit video recording.
- Neuroimaging studies e.g. Ct-scanning or MRI-brain.
- CSF examination to R/O infection, subarachnoid hemorrhage, demyelination disorder, and metabolic disorders.

✓ **Treatment of epilepsy:**

1) Ensure that the patient has a seizure disorder:
DD: Benign paroxysmal vertigo
Breath holding
Cough syncope
Familial choreoathetosis

Hereditary chin trembling
Shuddering attacks
Narcolepsy
Night terror
Pseudoseizures
Rage attack
Benign myoclonus of infancy
Tics.

2) Choosing an anticonvulsant based on the classification of the seizure.

➲ **Aim of treatment:**

Monotherapy with the fewest possible side effects for the control of seizures.

➲ **Routine monitoring of anticonvulsant levels to:**

1) At the onset of anticonvulsant therapy to confirm that the drug level is within therapeutic range.
2) For noncompliant patients and families.
3) At the time of status epilepticus.
4) During accelerated growth spurts.
5) For patients on polytherapy.
6) For uncontrolled seizures or seizures that have changed in type.
7) For symptoms and signs of drug toxicity.
8) For patients with hepatic or renal disease.
9) For children with cognitive or physical disabilities.

➲ **Benzodiazepines:**

Bind to a specific GABA site that enhances the opening frequency of the chloride channel without affecting open or burst duration.

➲ **Diazepam and lorazepam used for status epilepticus.**

➲ **Clonazepam:**

- Seizure type:
  - Absence.
  - Myoclonic.
  - Infantile spasms.
  - Partial.
  - Lennox-Gastaut.
  - Akinetic.
- Side effect: Drowsiness, irritability, agitation, behavioral abnormalities, depression, and excessive salivation.

➲ **Nitrazepam:**

- Seizure types:

Absence
Myoclonic
Infantile spasm

-Side effect:

is similar to clonazepam and hallucination.

➲ **Clobazam:**

It is used as an adjunctive therapy when seizures poorly controlled.

Side effect:

Dizziness, fatigue, weight gain, ataxia, and behavioral problems.

➲ **Carbamazepine:**

Acts by decreasing the sustained repetitive firing of neurons by blocking sodium-dependent channels and by decreasing depolarization- dependent calcium uptake

- Seizure type:

Generalized tonic clonic.
Partial.

- Side effect:

Dizziness, drowsiness, diplopia, liver dysfunction, anemia, neutropenia, SIADH, blood dyscrasias rare, and ***hepatotoxic effect***.

➲ **Ethosuximide:**

- Acts by blocking calcium channels associated with thalamocortical circuitry.

- Seizure type:

Absence
May increase tonic clonic seizures

- Side effect:

Abdominal discomfort, skin rash, liver dysfunction, and leukopenia

➲ **Gabapentin:**

Act by binding of the drug to neuronal membranes (glutamate synapses) and increased brain GABA turnover.

- Seizure type:
  - Adjunctive therapy when seizures poorly controlled.
- Side effect:

  Somnolence, dizziness, ataxia, headache, tremor, vomiting, nystagmus, fatigue, and weight gain.

➲ **Phenobarbital and primidone:**

- Seizure type:
  - Generalized tonic clonic.
  - Partial.
- Side effect:

  hyperactivity, irritability, short attention span, altered sleep pattern, Stevens-Johnson syndrome, depression of cognitive function.

➲ **Phenytoin:**

- Seizure type:
  - Generalized tonic clonic.
  - Partial.
- Side effect:

  hirsutism, gum hypertrophy, ataxia, skin rash, and Stevens-Johnson S.

➲ **Sodium valproate:**

- Seizure type:

  Generalized tonic clonic.
  Absence.
  Myoclonic.
  Partial.
- Side effect:

  weight gain, alopecia, hepatotoxicity, and tremor.

➲ **Ketogenic diet.**

➲ **Surgery for epilepsy.**

➲ **Counseling the parents.**

Hypotonia

- **Muscle tone:**
  - **Definition:** Muscle tone is the resistance to muscle stretch
    - *Phasic tone* (DTR)* or monosynaptic reflex elicited by rapid stretch of the muscle or tendon
    - *Postural tone* (antigravity) or amount of contraction induced by stretch influence of the gravity on the muscle

  *Deep Tendon Reflex

- **Hypotonia**
  - **Definition:** Reduction in postural tone with or without an alteration in phasic tone (DTRs)

- Differential anatomic diagnosis:
  - Brain
  - Spinal cord
  - Anterior horn cell
  - Peripheral nerve
  - Neuromuscular junction
  - Muscle fiber

- Physical examination:
  - Appearance (flaccid)
  - Traction response (head lag) → *normal up to 4 month*
  - Vertical suspension (slips through)
  - Horizontal suspension (drapes over) or inverted U-shape
  - "Scarf " sign → *if elbows cross midline consider it positive.*
  - Heel to ear or chin

  All these can't differentiate between central and peripheral hypotonia.

- Combined cerebral and motor unit hypotonia

  Mixed picture of peripheral and central hypotonia
  - Acid maltase deficiency → *inborn error of metabolism*
  - Congenital myotonic dystrophy
  - Congenital muscular dystrophies
  - Peroxisomal disorder
  - Lipid storage disease
  - Mitochondrial encephalomyopathies

- Neuroaxonal dystrophy
- Familial dysautonomia
- Asphyxia secondary to motor unit disease

♦ Cerebral hypotonia
- History consistent with a CNS insult
  - Convulsions within 1st 24hrs
  - Need for mechanical ventilation
  - Patient seems suppressed (very sleepy non-responding)
- Global developmental delay (gross motor, fine motor, cognitive, speech, and social)
- Microcephaly, dysmorphic features
- Malformation of other organs
- ***Weakness less than degree of hypotonia*** (non-paralytic hypotonia)
- Movement through postural reflexes.
- Brisk and/or persistent infantile (primitive) reflexes.
- DTRs: normal or brisk, ankle clonus, Babinski sign.
- Atrophy of muscle due to disuse

♦ Motor unit hypotonia
- No abnormalities of other organ or dysmorphic feature
- No global delay only delayed motor development
- Muscle atrophy, fasciculations
- Absent or depressed DTRs.

♦ **Causes of hypotonia**

General principles:
- Frequently medical rather than neurological or neuromuscular
- When not medical, more often caused by an abnormality of the UMN than LMN
- In certain instances, UMN and LMN abnormalities co-exist

Muscle tone determinants
- Gamma/Alpha motor system
- Visco-elastic properties of muscle
- Joint and tendon resistance

- **Systemic diseases (medical causes)**
  - Sepsis
  - Congenital heart disease
  - Hypothyroidism
  - Rickets
  - Malabsorption/malnutrition
  - Renal tubular acidosis

  Connective tissue disorders
  - Marfan syndrome
  - Ehlers-Danlos syndrome
  - Congenital laxity of ligaments

- **Cerebral hypotonia causes:**
  - Chromosomal disorders
  - Down syndrome
  - Prader-Willi syndrome
    - FTT, severe hypotonia,
    - When grow up become polyphagic → *obese, mental* retarded and cryptorchism
  - Other genetic defects
  - Acute hemorrhagic and other brain injury
  - Hypoxic/ischemic encephalopathy (HIE)
  - Chronic non-progressive encephalopathy
  - Peroxisomal disorders
  - Metabolic defects
  - Drug intoxication
    - E.g. mother received anesthesia, narcotics, MgSO4
    - "Benign" congenital hypotonia

      Patient catch up as he or she grows up
      They have learning and behavioral problems later.

- **Spinal cord injury:**
  - Breech presentation
  - Cephalic presentation

- **Motor unit hypotonia**
  - *Anterior horn cell*
    1. Spinal muscular atrophy (SMA)
    2. Poliomyelitis
    3. Neurogenic arthrogryposis
    4. Incontinentia pigmenti

- *Nerve root/Peripheral nerve*
  1. Guillain-Barre syndrome
  2. Chronic inflammatory demyelinating polyneuropathy
  3. Congenital hypomyelinating and axonal neuropathy
  4. Hereditary motor-sensory neuropathies

- *Neuro muscular junction*
  1. Neonatal myasthenia
  2. Congenital myasthenia and myasthenic syndromes
  3. Infantile botulism

- *Muscle*
  1. Congenital muscular dystrophy
  2. Congenital myotonic dystrophy
  3. Congenital myopathies
  4. Metabolic myopathies
  5. Infantile myositis

➢ **Clinical hints:**

- Obtain detailed history of:
  - Gestational (fetal movement, weight gain of the mother to rule out polyhydramnios because of weak baby is not able to swallow fluid)
  - Perinatal (prolong labor due to myotonic dystrophy of the mother uterus)
  - Postnatal
- Somatic abnormalities, especially of head and lack of normal social and adaptive responses are indicative of UMN hypotonia.
- With LMN hypotonia; children look "bright", with normal social and adaptive responses.
- Deep tendon reflexes (DTRs) are usually preserved in UMN hypotonia except with acute encephalopathies.
- With LMN hypotonia, muscle weakness and depressed or absent DTRs are often found.

Hypotonia is a sign whose cause may be medical rather than neurological or neuromuscular
When not medical is more often due to an abnormality of the UMN than of the LMN.
Neuromuscular diseases in the newborn period present primarily with hypotonia and weakness.

- Infant with severe hypotonia but only marginal weakness usually don' t have a disorder of the LMN like AHC (anterior horn cell) and peripheral or cranial nerves and neuromuscular junction and muscle.
  These infant may have:
  - Genetic condition
  - Metabolic disturbances
  - Congenital heart disease
  - Hypothyroidism
  - Sepsis
  - Other systemic disorder

- Infant with CNS pathology may present with profound hypotonia, decreased reflexes and moderate to severe but transient weakness, however they also tend to have seizures, obtundation and cranial nerves signs and/or history of perinatal asphyxia.
  Then with recovery, they gradually develop better strength increased reflexes and muscle tone distally first, in contrast to asphyxiated infants with disorders of LMN in whom the weakness, hypotonia and hyporeflexia are present.

- Alternatively profound weakness and hypotonia without signs of CNS involvement occur in newborn infants with isolated neuromuscular disease and no history of perinatal asphyxia.

- DTRs vary depending on the anatomical level of pathology along motor unit
  i.e. prominent hyporeflexia or total areflexia in neuropathies and
  Almost normal reflexes in neuromuscular junction defects and in myopathies

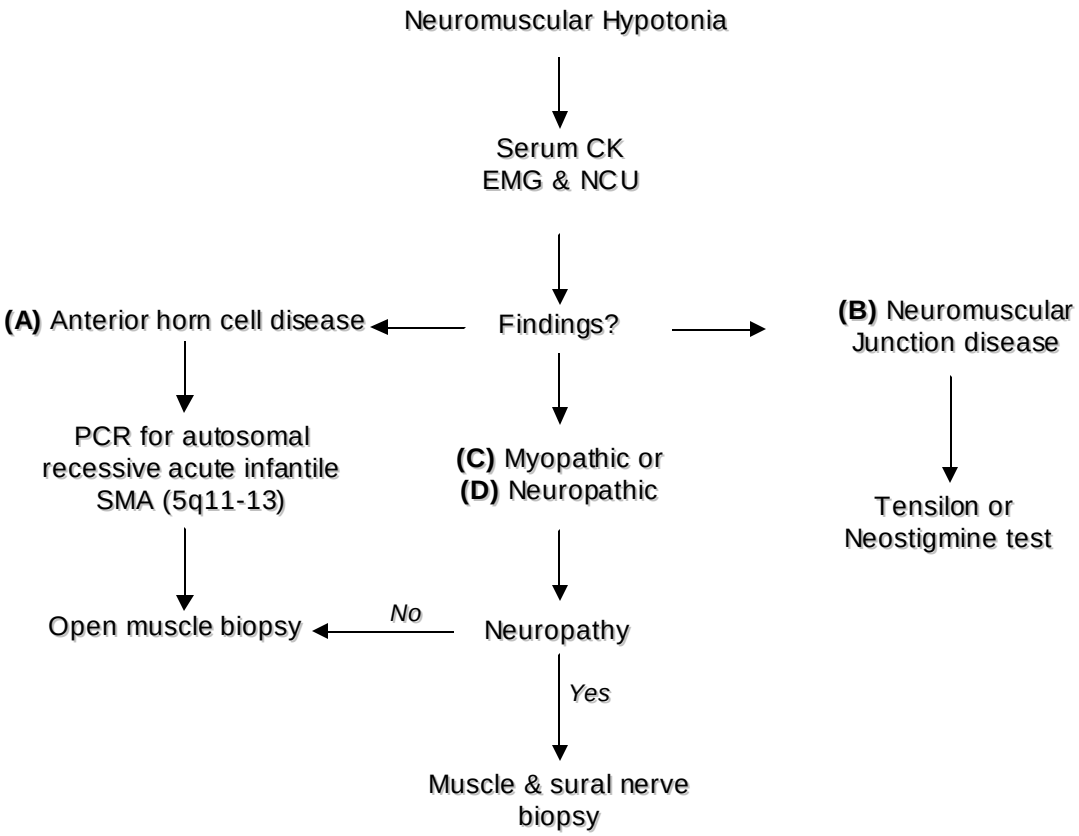
- **Investigations:**

If a motor unit disorder is suspected in newborn infant the mother should be questioned for history (symptoms) and examined (sign) for myasthenia gravis or myotonic muscular dystrophy
if –ve → *then do:*

- CPK → Elevated in myopathies
  Congenital muscular dystrophy
  Trauma to muscle (elevated in 1st week due to passing through the birth canal)
- Electrolytes → *especially K*

- Lactate
- Pyruvate
- Uric acid
- Creatinine and aldolase → *muscle enzymes*
- Cholinesterase inhibitors (for myasthenia gravis, can lead to bradycardia so need monitoring)
    - Edrophonium chloride or
    - Neostigmine test along with EMG/NCS (nerve conduction study)

- Muscle biopsy appropriate biochemical and/or genetic test should be ordered
- Nerve biopsy and muscle biopsy for histologic, immunohistochemical, biochemical or genetic analysis.



On EMG:
(A): neurogenic pattern (wide and large motor unit) b/c atrophy of muscle
(B): electrodescement pattern on repetitive muscle stimulator
(C): myopathic pattern (motor unit are short and large)
(D): myopathic and neurogenic pattern

➢ Evaluation of neuromuscular hypotonia

Genetics disorders of neuromuscular hypotonia

SMA (Spinal Motor Atrophy)
- Werdnig-Hoffmann disease (AR) → *5q11*-13
- Kugel Berg-Walander disease (AR) → *5q11*-13

Congenital myopathies
- Central core disease → *19q13*
- Myotubular myopathy → *αq28*
- Nemaline rod myopathy → *19 21*-23
- Congenital fiber type disproportion trans 10p11:17q25

Muscular dystrophies
- Congenital myotonic dystrophy → *19q13*
- Merosin-deficient muscular dystrophy → *6q2*
- Fukuyama congenital muscular dystrophy → *9q31*-32

Metabolic myopathy
- Pompe's disease (acid maltase deficiency) → *17q23*
- Phosphofructokinase → *1 cen q32*

➲ *Spinal Motor Atrophy (SMA)*

- AR & due to degeneration of anterior horn cell
- Progressive weakness & wasting of skeletal muscles
- The 2nd most common cause of neuromuscular disease in the UK after DMD (Duchenne Muscular Dystrophy)

a) Type-I SMA (Werdnig-Hoffmann disease)
- Progressive disorder presenting in early infancy (0-6 month)
- Decrease fetal movement
- Fasciculation of the tongue
- Intercostal recession due to weakness of respiratory muscle
- Lack of antigravity power in hip flexures
- Absent DTRs
- Arthrogryposis (positional deformities of the limbs)
- Death 2ry to respiratory failure by 12 months of age

b) Type-II SMA (intermediate type)

- Present between 6-18 months of age
- Most will be able to sit but few will walk
- Die by toddler

c) Type-III SMA (Kugel Berg-Wanlander disease)

- Present after 18 months of age
- Most can walk but have problems of skeletal muscle (atrophy, scoliosis & skeletal deformities)

➲ ***Myasthenia gravis:***

Abnormal muscle fatigability which improves with rest or anticholinesterase drugs

➢ Transient neonatal myasthenia:

- Seen in 10% of infants born to mothers with Myasthenia Gravis
- Due to anti-acetylcholine ABs crossing the placenta
- Difficulty in feeding, muscular weakness, respiratory insufficiently for 2-3 weeks of age.

➲ ***Muscle disorders***

➢ Congenital muscular dystrophies:

- Muscle weakness at birth or early infancy
- AR
- Often non progressive
- Muscle biopsy: histological changes similar to those seen in other muscular dystrophy. Also genetic testing is available.

➲ ***Myotonic disorders:***
Myotonia is delayed relaxation after sustained muscle contraction

- Dystrophia myotonica
  - AD inheritance
  - Newborn presents with profound hypotonia, feeding difficulty and intermittent respiratory difficulty.
  - Mother is usually affected
  - Learning difficulties, expressionless face
  - Distal wasting and myotonia
  - Cataract
  - Baldness and testicular atrophy in males
  - Death due to cardiomyopathy

➲ ***Metabolic myopathies:***
- In infancy: hypotonia
- In older children: muscle weakness or cramps in exercise
  E.g.
  - Glycogen storage disorder.
  - Muscle lipid disorders, affecting oxidation of FA, a major source of energy for skeletal muscle
  - Mitochondrial cytopathy (multisystem with LA and encephalopathy)
  - Pompe's disease (acid maltase deficiency) present with CM, hepatosplenomegaly, large tongue and muscle involvement.

➲ ***Congenital myopathies:-***
- e.g. Central core
  Nemaline rod
  Diagnosed by muscle biopsy
- CPK can be normal or elevated
- EMG & NCS show myopathic charges
- Early on can be normal

➲ ***Central hypotonia***
- Neuroimaging: CT brain, MRI, US for hemorrhage
- CSF to role out infection
- EEG if the patient has seizures
- Electrolyte

- LFT
- Bilirubin → *for kernicterus*
- Lactic acid→ *for metabolic*
- Signs of hypoxic brain insult
- Sign of dysmorphic features
  FISH for chromosome 15 → *Prader*-Willi syndrome
- Screening for metabolic disorders:
  Amino acids, organic acid very long chain fatty acids, lactic acid, pneumonia, and ABG to role out acidosis.

Further reading
http://www.enmc.org

Rheumatic fever الحمى الرثويّة

✓ **Incidence:**

If there are 100 patients with pharyngitis (due to streptococcus) and not treated, 3 of them may develop rheumatic fever (3%)

✓ **Age:**

5-15 years old (why?) b/c streptococcal infection is common among this age

✓ **Pathophysiology:**

Is related to an immune reaction to untreated group A beta-hemolytic streptococcus infection.

✓ **Incubation period:**

1-5 weeks and even the symptoms may appear after 6 months of exposure as in Sydenham' s chorea

✓ **Symptoms:**

Criteria in Jones system (purely clinical)

➢ Major criteria:

1-On Heart: could be

Endocarditis: mostly of left side (mitral valve as well as the aorta)
Myocarditis
Pericarditis
Signs of heart affection by rheumatic fever:

- Continuous tachycardia
- Murmurs (due to mitral or aortic regurgitation)
- Friction rub
- Signs of heart failure

2-On Joints:

Signs of arthritis due to rheumatic fever

- Migratory arthritis
- Severe tenderness
- Affect medium – large joints
- Extremely response to salicylate within 24-48 h

3-On CNS:

Sydenham' s chorea: characterized by:

- Adolescence
- Psychological disturbances
- Purposeless movements affect limb

4-On Skin:

- Erythema marginatum
- Subcutaneous nodules

➢ Minor criteria:

- Fever: temperature elevation
- Arthralgia: Joint pain without swelling
- Laboratory abnormalities: increased Erythrocyte sedimentation rate, increased C reactive protein, leukocytosis
- Electrocardiogram abnormalities: a prolonged PR interval
- Evidence of Group A Strep infection: positive culture for Group A Strep, elevated or rising Antistreptolysin O titre
- Previous rheumatic fever or inactive heart disease

✓ **Diagnosis:**

By two major criteria, or one major and two minor criteria

What we need to prove the diagnosis?

Evidence of streptococcal infection:

- +ve ASO titer (serology)
- Blood culture (Bacteriology)
- Scarlet fever

There are 2 conditions where there is no need to find an evidence of streptococcal infection (according to WHO 1992):

- Sydenham' s chorea
- Patient accidentally found to have Pansystolic murmur at the apex and nothing else to suggest otherwise consider this patient has previous rheumatic fever and this is one of its sequela

- ✓ **Management:**

Acute management:

Admission with complete bed rest

Penicillin → to eradicate any remnant of streptococcus organisms

Specific:

Arthritis → salicylate

Heart: depend on the severity

Mild involvement→ salicylate

Moderate to severe → steroid

N.B. don' t treat any patient as rheumatic fever unless you are 100% confidant about the diagnosis. So if you are not sure you can give the patient paracetamol instead of salicylate b/c salicylate may ameliorate the condition but may change the presentation while paracetamol will have only analgesic effect without anti-inflammatory. Also whenever the patient diagnosed to have rheumatic fever he will be kept on long course of prophylactic antibiotic so, be sure about the diagnosis.

Prophylaxis:

Benzoyl penicillin (IM):

For how long should the patient take the prophylaxis?

There are 3 patterns:

- 5years from last attach
- Up to 18 years
- Forever

N.B. but we see the situation and the job of the patient; if he has regular contact with others (teacher, soldier ..) he must continue to take prophylaxis.

Heart failure

✓ **Definition:**

It is the inability to bump the blood forward from the left side as well as failure to dispense the venous return.

✓ **Causes:**

➢ Fetal:

- Anemia: hemolytic, aplastic
- Arrhythmia (treated by digoxin)

➢ After birth:

- Congenital heart disease: most commonly left to right shunt

N.B. Tetralogy of Fallot is rarely cause heart failure

✓ **Symptoms:**

There are 4 cardinal signs of heart failure:

- Tachycardia
- Tachypnea
- Hepatomegaly
- Edema

✓ **Diagnosis:**

The diagnosis is made clinically

✓ **Treatment:**

➢ general:

- Admission with rest on 45^{o} position
- Provide O_2
- Restricted fluids
- Support the input output chart
- Negative inotropic factors have to be corrected (acidosis, hypoxia, hypoglycemia, hypocalcemia)

➢ Specific:

Depend on the cause of heart failure

- Decrease the preload (preload medications): diuretics
- Decrease afterload (afterload medications): ACEI
- Inotropic: digoxin, if the patient get worse → dopamine, dobutamine

Kawasaki disease

(Mucocutaneous Lymph Node Syndrome)

✓ **Introduction:**

- Kawasaki syndrome, is a poorly understood self-limited vasculitis that affects many organs, including the skin and mucous membranes, lymph nodes, blood vessel walls, and the heart. It does not seem to be contagious. It was first described in 1967 by Dr. Tomisaku Kawasaki in Japan.
- The causative agent of Kawasaki disease is still unknown. However, current etiological theories center primarily on immunological causes for the disease. Much research is being performed to discover a definitive toxin or antigenic substance, possibly a super antigen that is the specific cause of the disease. An unknown virus may play a role as an inciting factor as well.
- The cardiac complications are, by far, the most important aspect of the disease. Kawasaki disease can cause vasculitic changes (inflammation of blood vessels) in the coronary arteries and subsequent coronary artery aneurysms. These aneurysms can lead to myocardial infarction (heart attack) even in young children. Overall, about 20% of children with Kawasaki disease develop coronary artery aneurysms.

✓ **Race**: The disease is more common in the Japanese-American population.

✓ **Sex:** The disease is more common in males than in females, with a male-to-female ratio of 1.5:1.

✓ **Symptoms**

- High-grade fever (greater than 39 °C or 102 °F; often as high as 40 °C or 104 °F) that normally lasts for more than a week if left untreated.
- Red eyes (conjunctivitis) without pus or drainage, also known as "conjunctival injection"
- Bright red, chapped, or cracked lips
- Red mucous membranes in the mouth

- Strawberry tongue, white coating on the tongue or prominent red bumps (papillae) on the back of the tongue
- Red palms of the hands and the soles of the feet
- Swollen hands and feet
- Rash which may take many forms, but not vesicular (blister-like), on the trunk
- Swollen lymph nodes (frequently only one lymph node is swollen), particularly in the neck area
- Joint pain (arthralgia) and swelling, frequently symmetrical
- Irritability
- Tachycardia (rapid heart beat)
- Peeling palms and soles (later in the illness); peeling may begin around the nails

✓ **Signs and tests**

A physical examination will demonstrate many of the features listed above.

➢ Blood tests
- Complete blood count (CBC) may reveal leukocytosis, normocytic anemia and eventually thrombocytosis
- Erythrocyte sedimentation rate (ESR) will be elevated
- C-reactive protein (CRP) will be elevated
- Liver function tests may show evidence of hepatic inflammation and low albumin

➢ Other tests (may or may not be performed)
- Electrocardiogram may show evidence of ventricular dysfunction or, occasionally, arrhythmia due to myocarditis
- Echocardiogram may show subtle coronary artery changes or, later, true aneurysms.
- Ultrasound or computerized tomography may show hydrops (enlargement) of the gallbladder
- Urinalysis may show white blood cells and protein in the urine (pyuria and proteinuria) without evidence of bacterial growth
- Lumbar puncture may show evidence of aseptic meningitis
- Angiography was historically used to detect coronary artery aneurysms and remains the gold standard for their

detection, but is rarely used today unless coronary artery aneurysms have already been detected by echocardiography.

✓ **Diagnosis:**

Five of six criteria are needed for diagnosis:

1. Fever persisting for 5 days or more
2. Changes of peripheral extremities:
    a. Initial stage: reddening of palms and soles, indurative edema
    b. Convalescent stage: membranous desquamation from fingertips
3. Polymorphous exanthem
4. Bilateral conjunctival congestion
5. Changes of lips and oral cavity: reddening of lips, strawberry tongue, and diffuse injection of oral and pharyngeal mucosa.
6. Acute, non-purulent cervical lymphadenopathy (>1.5 cm in diameter)

✓ **Management:**

- It is imperative that treatment be started as soon as the diagnosis is made to prevent damage to the coronary arteries.
- Intravenous gamma globulin (IVIG) is the standard treatment for Kawasaki disease and is administered in high doses with marked improvement usually noted within 24 hours.
- Salicylate therapy, particularly aspirin, remains an important part of the treatment but salicylates alone are not as effective as IV gamma globulin. Aspirin therapy is started at high doses until the fever subsides, and then is continued at a low dose for its effect in preventing platelet aggregation and thrombosis. Except for Kawasaki disease and a couple of other indications, aspirin is otherwise normally not recommended for children due to its association with Reye's syndrome.

Neonatal respiratory distress

- What are the signs of respiratory distress?
  1) Tachypnea: respiratory rate > 60/min
  2) Grunting: an expiratory noise made by neonates with respiratory problems. It generally occurs throughout the expiratory phase of breathing, and represents breath against a partially closed glottis. This maintains a high pressure and prevents alveolar collapse.
  3) Flaring of ala nasi
  4) Cyanosis (what are the differential diagnosis of cyanosis?)
     - Cardiac problem e.g. cyanotic congenital heart diseases
     - Respiratory problem
  5) Retraction of intercostal muscles
  6) Using of accessory respiratory muscles
  7) Tachycardia
  8) Wheezing

- What is the definition of neonate?
  Any baby born in term up to 28 days.

- What is the definition of prematurity?
  It is the period from the age of the viability till last day of 37^{th} week of pregnancy.

- What are the causes of respiratory distress in neonate?

1- Surfactant deficiency due to prematurity:

- This is the most common cause of respiratory distress in neonate
- The timing of surfactant (lecithin) production in quantities sufficient to prevent atelectasis depends on an increase in fetal cortisol level that begins between 32 & 34 weeks of gestation.

- What are the components of surfactant?
  - Phospholipid (lecithin): which represent 90% of the surfactant and is responsible of decrease the surface tension created by fluids in the alveoli.
  - Protein: helps in spread of the phospholipid.

- Could the baby have respiratory distress without lung pathology?
  Yes in:
  - Anemia
  - Sepsis
  - Acidosis
  - Febrile baby

- What should be done with a mother having premature contraction (e.g. 24 weeks)?
  Steroid should be given (not more than 2 courses to avoid brain hypoplasia & growth restriction)

- What are the factors that enhance surfactant maturation?
  - Steroid: enhance maturation of bar body which produces surfactants.
  - Smoking.
  - Preeclampsia: enhancement of internal corticosteroid secretion.
  - Premature rapture of membrane.

- What is the incidence of respiratory distress in 100 babies?
  - If they are term babies: 1-3%
  - If they are premature: as the age increased the incidence of respiratory distress decrease.

2- meconium aspiration syndrome:

- How it cause respiratory distress?
  - Deactivation of the surfactants: treated by exogenous surfactant
  - One valve obstruction
  - Chemical pneumonia

- Why the babies pass meconium in-utero?
  Because he is in distress, about 12% of babies pass meconium in-utero but only 5% will have meconium aspiration syndrome.

➲ What are the physical signs of meconium aspiration syndrome?
- Term or mostly post-term baby
- Distressed baby
- Meconium (yellowish in color) can be detected under nails, axilla, inside the ears and umbilicus

3- Neonatal pneumonia (early sepsis):

Signs of neonatal sepsis could be classify into:
- Very early
- Early
- Late
- Late late
- Very late late

Pneumonia is a one of early signs of neonatal sepsis.

➲ Which organisms could cause pneumonia (early sepsis) in neonate?
- Group B G +ve streptococci
- Listeria
- G –ve (E.coli)
- Non-typable H.influenza
- Enterococcus

➲ What are the indications for intubation?
- To give medication
- To give surfactants
- To aspirate meconium
- Diaphragmatic hernia
- To control chest compression

4- persist pulmonary hypertension (persist fetal circulation):
- Mostly happened with term babies
- Treated by vasodilator (nitric oxide which selective pulmonary vasodilator which is discovered at 1999)

5- Diaphragmatic hernia
- Viscera from abdomen press on the lungs (space occupying lesion) and cause respiratory distress.
- Diagnosed by chest x-ray

6- Air leak syndrome

- Where are the sites of air leakage?
  - In the lung → pulmonary interstitial emphysema (air leaks and becomes trapped between the alveoli), lobar emphysema
  - In the pleura → pneumothorax
  - In the mediastinum → pneumomediastinum
  - In the pericardium → pneumopericardium
- How to diagnose pneumothorax clinically?
  - By transillumination
  - Treatment: aspiration

7- Pulmonary hemorrhage

- Predisposing factors:
- Prematurity
- PDA
- Side effect of administration of exogenous surfactant

- Symptoms:
  The onset of P-Hem is characterized by oozing of bloody fluid from the nose and mouth or endotracheal tube with associated rapid worsening of the respiratory status, cyanosis and, in severe cases, shock.

- How does it cause respiratory distress?
  The blood deactivates surfactant in the lung.

8- Pulmonary hypoplasia

- Predisposing factors:
  - Severe maternal oligohydramnios (little amniotic fluid → little amniotic fluid taken by the baby → little AF will go to the lungs → hypoplasia)
    N.B. Part of amniotic fluid taken by the baby is excreted by the kidneys and part will go to the lungs leading to expansion & dilation of the lungs
- Management: high frequency oscillator.

9- Transient tachypnea of newborn (TTN)

- **Old theory:** Before birth, the lungs of the fetus are filled with fluid. While a fetus is inside of its mother, it does not

use its lungs to breathe - all its oxygen comes from the blood vessels of the placenta.

- During the birthing process, as a baby passes through the birth canal, some of the fluid inside the baby's lungs is "squeezed" out. After the birth, during the first breaths that a newborn takes, the lungs fill with air and more fluid is pushed out of the lungs. Any remaining fluid is then coughed out or gradually absorbed into the body through the bloodstream.
- In infants with TTN, however, there is extra fluid in the lungs or the fluid in the lungs is absorbed too slowly. As a result, it is more difficult for the baby to take in oxygen properly, and the baby breathes faster and harder to compensate. The condition typically lasts between 24 to 72 hours.

➢ Management: CPAP

- **New theory**: active chloride pump channel is responsible for fluid release in the lung from the cell to outside (through active process)
  These patients with Transient tachypnea of newborn have abnormal active chloride pump channel. What support this that many babies who born by cesarean section not have TTN.
  Moreover, many normal vaginal delivery babies have TTN.

➲ Is there any drug when it given to the mother can cause respiratory distress? (MCQ in this area)

- There is no drug given to the mother and cause respiratory distress
- If the mother receives pethidin –for sedation- it may pass to the baby if they given it 4 hours and causes apnea, in this case the management is by given naloxone to the baby (IV, IM)

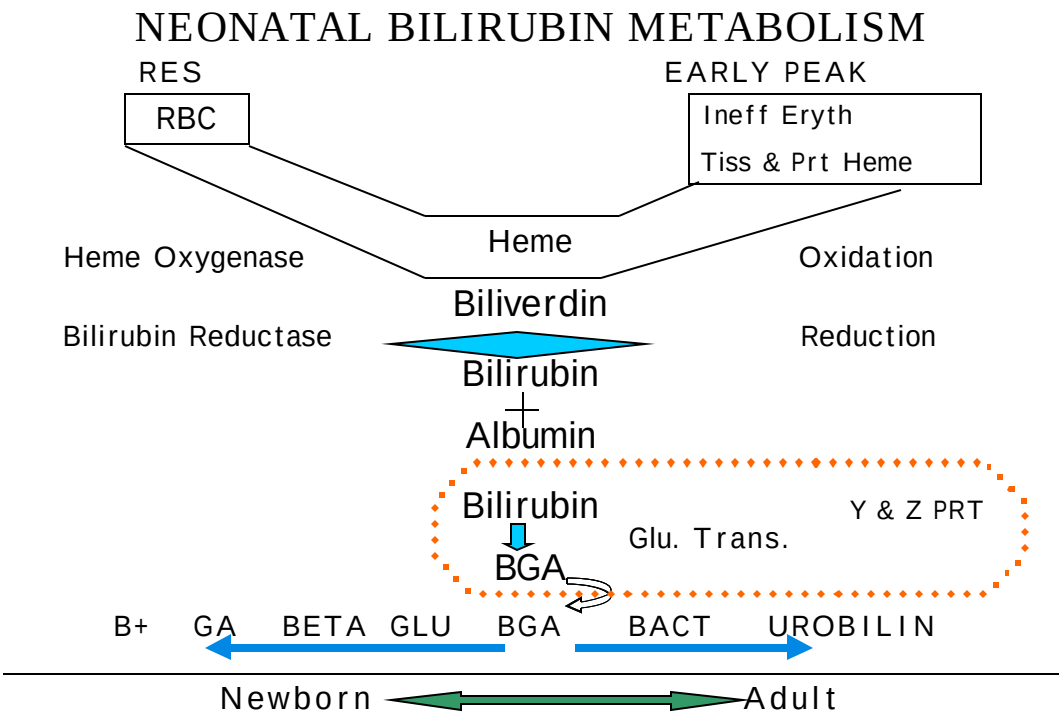
Neonatal Jaundice

✓ **Definition:**

It is pigmentation of skin & mucus membranes due to increase concentration of bilirubin in the blood.

✓ **Importance**

- Can have dangerous effect.
- Can guide us to the underlying abnormality.



✓ **Categories of Neonatal Hyperbilirubinemia:**

➢ Types of bilirubin:

- unconjugated
- conjugated

➢ Types of jaundice:

- physiologic
- pathologic

✓ **Physiologic Jaundice:**

- Jaundice in the newborn.
- Usually noticed after 24 hrs. of life and not last more than 8 days.
- Mean peak bilirubin 8 mg% but may reach 12mg%.
- Not increased by more than 5mg/dl/day
- Not associated with kernicterus or any neurodevelopmental abnormality.

➢ Factors contributing to physiologic jaundice:

- Increased bilirubin load to liver.
- Decreased ability to clear bilirubin from plasma.
- Defective conjugation and excretion.

✓ **Pathological jaundice:**

- Jaundice in the first 24 hrs. of life.
- Serum bilirubin over 12mg%.
- Jaundice persisting more than 8 days.
- Direct bilirubin over 1.5mg%.
- Rapidly increasing bilirubin, over 5mg/dl/day.

✓ **Classification of jaundice by the type of bilirubin:**

➢ Indirect

- Mostly increased bilirubin load

➢ Mixed

- Hepatic dysfunction (conj. <40%)
- Biliary tract obstruction (conj. >50%)

➢ Causes of Unconjugated Hyperbilirubinemia:

- Excessive production due to:

➢ Hemolysis:

- ABO incompatibility: mediated by (IgM) antibodies which are produced naturally according to presence of A&B antigens on the RBCs (in vivo)
- RH incompatibility: mediated by (IgG) [need sensitization] [in vitro]

- Enzyme deficiency, e.g. G6PD → hemolysis in fever & infection
- Spherocytosis

➢ ↑ RBCs – polycythemia
➢ Extravascular blood – hematoma – swallowed blood

- Increased enterohepatic circulation:
  - ➢ Delayed feeding → stasis →↑ absorption
  - ➢ Intestinal obstruction
  - ➢ *Breast milk (β*-gluconidase)
- Inadequate hepatic metabolism:
  - ➢ Prematurity
  - ➢ IDM (↑insulin), hypothyroid
  - ➢ Glucoronyl transferase deficiency

➢ Factors that suggest the possibility of hemolytic disease:
- Family history of significant hemolytic disease.
- A rise in serum bilirubin of >0.5 mg/dl/h
- Pallor/Hepatosplenomegaly
- Rapid increase in the TSH level after 24-48H (consider G6PD deficiency)
- Ethnicity suggestive of inherited disease
- Failure of phototherapy to lower the TSB level

➢ Causes of mixed hyperbilirubinemia:
- Hepatic damage
  1) Hepatitis
  2) Septicemia
  3) Hypoxia

- Obstruction of biliary tree
  1) Extrahepatic-biliary atresia
  2) Intrahepatic-hepatitis

Signs of cholestatic jaundice:
- Dark urine
- Urine positive for bilirubin
- Light-colored stools
- Persistent jaundice for >3 weeks

✓ **Management of Hyperbilirubinemia:**

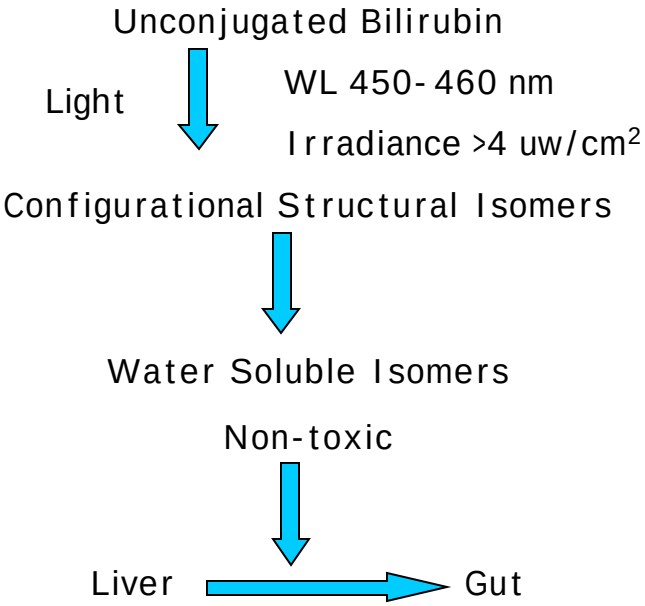
- History and examination
- Investigation: blood, urine, others
- Reduce rise of bilirubin
  a) Identify susceptibility
  b) Treat specific cause
  c) Phototherapy
  d) Exchange blood transfusion

- Clinical signs suggestive of the possibility of other diseases in which jaundice may be one manifestation of the disease such as sepsis or galactosemia:
  - Vomiting
  - Lethargy
  - Poor feeding
  - Hepatosplenomegaly
  - Excessive weight loss
  - Apnea
  - Temperature instability
  - Tachypnea
  - Reduction of Bilirubin Level

Treatment	Category of Infant	Level of Unconj. Bilirubin
EBT	Term	20 mg/dl
	Low birth weight	10-18 mg/dl
Phototherapy	Term	5 mg less than
	Low birth weight	EBT level

- Factors to consider:
  - Birthweight or gestation
  - Level of unconjugated bilirubin
  - Postnatal age
  - Cause of jaundice
  - Other risk factors for kernicterus

PHOTOTHERAPY



- Complications of Phototherapy:
  - Retinal damage
  - Skin rash
  - Pyrexia
  - Fluid loss
  - "Bronze baby"

- Exchange Blood Transfusion
  - ***Physiology***
    1. Correct anemia
    2. Hyperbilirubinemia (2 vol EBT)

  - ***Procedure***
    1. Blood
    2. Technique
    3. Monitor
    4. Time

  - ***Complications***

Metabolic	Vascular	Cardiac
Infection	Bleeding	Others

The Child with a Murmur

✓ **Definition**

It is an audible turbulent sound wave which emits from the heart and its valves within 20-20,000 Hz.

✓ **Types**

1- Systolic: occurs between 1st and 2nd heart sounds.
   - Ejection systolic: forward ejection of blood from ventricles through semilunar valves to the arteries, it takes a diamond shape in phonocardiogram.
   - Regurgitant systolic: from ventricles through AV valves or through VSD.
   - Pansystolic.

2- Diastolic: between 2nd and 1st heart sounds.

✓ **Grades**

The loudness of a murmur depends on:

1- Pressure gradient.
2- Volume of blood flow.

✓ **Classes :**

Depend on significance:

1- Significant (pathologic).
   a- Acquired.
   b- Congenital.
2- Insignificant (non-pathologic – innocent) 50%
   - Factors which make the murmur heard more frequently include Tachycardia caused by for example anemia, anxiety, fever, etc.
   - There are about 5 types of innocent murmurs, but the most important (commonest) are:
     1- Still's murmur
        @ Ejection
        @ Vibratory
        @ Normal heart and lung field on CXR
        @ Normal ECG
        @ Confined to the precordium (no radiation)
        @ Change with position
     2- Venous hum
     3- Mammary soufflé

Congenital heart disease (CHD)

ACYANOTIC (⅔)		CYANOTIC	
Lt → Rt shunt	**Obstructive**	↓ PBF	↑ PBF
50% of all CHD VSD PDA ASD	AS PS	Tetralogy of Fallot	Transposition of great arteries

✓ Incidence of CHD:

0.9 – 1 %

✓ Predisposing factors:

- Maternal factors:
  - ✓ Diabetic mother
  - ✓ Drug consumption
  - ✓ Radiation exposure
  - ✓ Infections e.g. (rubella)
- Baby factors:
  - ✓ Chromosomal abnormalities

Fetal circulation

✓ Before birth:

The blood passes from the placenta through the umbilical vein with O_2 saturation 30-35 mmHg (this is considered highly oxygenated), 50% of this blood will go to the liver and the rest will bypass the liver through ductus venosus and will join the inferior vena cava. This amount of blood, with the blood coming from lower portion of the body will make the saturation in the right atrium 26-28 mmHg and will preferentially pass through the foramen ovale to the left atrium → left ventricle → aorta → to the upper portion of the body. 90% of this full saturated blood will go to the head and upper portion of the body and only 10% will pass the isthmus and go down through descending aorta.

The superior vena cava carries the poorly saturated blood (12-14 mmHg). It will pass to the right atrium and preferentially will pass through the tricuspid valve to the right ventricle (the saturation will increase to 16-18 mmHg). This amount of blood will be pumped through the pulmonary artery. Because the pulmonary circulation is constricted, the majority of this blood will bypass the lungs through PDA to the descending aorta (90%), only 10% will go to the lungs. 2/3 of the blood coming through the descending aorta will go back to the placenta to be resaturated. Only 1/3 will go to the lower body organs.

✓ **After birth**

As soon as the baby born, the 1st breath will make the lungs inflate (so the 1st cause of pulmonary circulation constriction is gone).

2nd: Is hypoxia (30-35 mmHg)

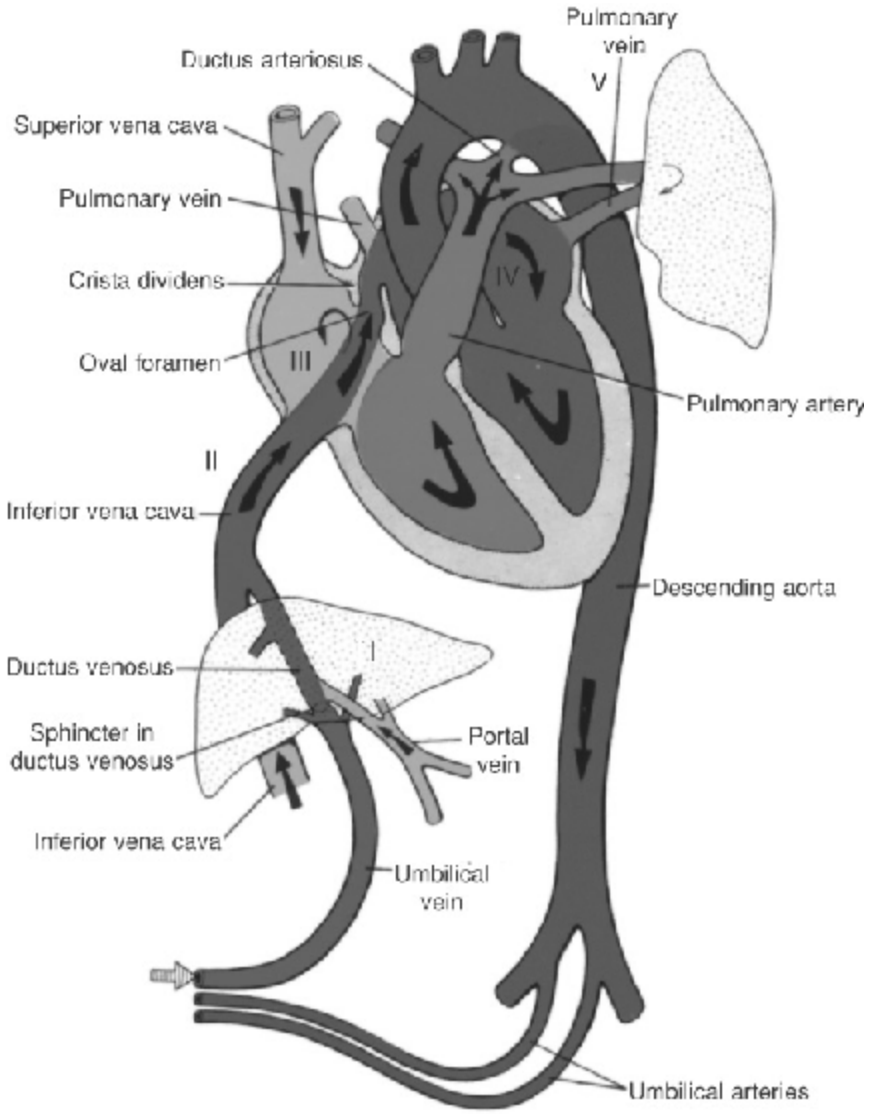
3rd: Is hypertrophy of pulmonary vessels (This takes 6-8 weeks to release)

- When the baby takes O2 by nose, this will increase the saturation to 60 mmHg, so this will release the 2nd cause.

(1) When the placenta is eliminated, the pressure in the systemic fetal arteries as well as aorta will increase → ↑ pressure in the Lt atrium.

(2) At the same time, because there is no blood coming through umbilical vein, pressure in Rt atrium .

- These 2 events will lead to closure of foramen ovale, but in 20-30% of adults, it will remain somewhat open that a probe can be passed through it.
- Because no blood passes through ductus venosus, it will close.



- **<u>Acyanotic Congenital Heart Disease</u>**

(A) Lt → Rt shunt lesions

- **Pathophysiology and symptoms:** due to the effect on lungs and heart

N.B. the volume of blood in the pulmonary circulation should be ≥ 1.5 times as the systemic circulation to have symptoms. (Certain lesions can give 2-3 times).

The symptoms also depend on the size of the lesion.

↑*Pulmonary blood flow*→congestion of lungs→↓*compliance*→dyspnea on exertion

→ Repeated chest infection

→ Leakage → pulmonary edema tachypnea

↑ *blood return to Lt ventricle* → significant amount will go to Rt ventricle
→ ↓ *blood to systemic circulation* → (compensation by ↑ *heart rate* or ventricular enlargement) ↑ *catecholamine production.*
→ ↑ *heart rate &* ↑*energy consumption* → ↓*body weight* (failure to thrive)
→ if this persists the patient may fall in *frankly heart failure*.
→ ↑ *catecholamines* → peripheral vasoconstriction → increase core temperature
→ profusely sweating over the head.

- **What are the factors that** ↓ *symptoms?*
  - Pulmonary vascular pressure (which results from hypertrophy of pulmonary vessels) {after birth, ↑ *O2 and the* lungs work}
  - Small lesion

N.B. The hypertrophy of pulmonary vessels need 6-8 weeks to become normal & until that time, the patient will not have symptoms.
EXCEPT. # multiple lesions
premature baby
N.B. long standing Lt → Rt shunting →→ histological changes over the pulmonary arterioles (thickness & stiffness).
→ ↑ *resistance & pressure* → hypertrophy of Rt ventricle → Rt→Lt shunt (this is called pulmonary vascular disease & Eisenmenger complex).
This mostly occurs at the 2nd decade except for the patient with Down's syndrome whom may develop these changes at 2nd year of life.

(1) Ventricular Septal Defect (VSD)

✓ **Incidence:**
- 30-35% of all CHD (the most common CHD)

✓ **Types:**
- Perimembranous (most cases)
- Muscular
- Membranous

✓ **Symptoms:**
- Same

✓ **Clinically:**
- Hyperdynamic precordium (thrill over mid Lt parasternal side)
- Pansystolic murmur
- Mid diastolic murmur (due to relative mitral stenosis) N.B. previously before ECHO they depend on this sign in follow up. When rumbling decrease, either:
  1- the lesion starts to close.
  2- Pulmonary vascular disease.

✓ **Investigations:**
- Chest X-Ray.
  # Cardiomegaly
    * if it is of Lt side → obliteration of retrocardiac space
    * if it is of Rt side → obliteration of retrosternal space
  # pulmonary congestion
- ECHO the diagnostic tool

✓ **Management:**
- N.B. The small size & muscular type of VSD has better chance to close by 1st-2nd year.
- till that happen → manage heart failure with good feeding.
- Usually babies are sent to surgery by 6-9 months.

✓ **Complications**
1- pulmonary vascular disease
2- subacute bacterial endocarditis

(2) Patent Ductus Arteriosus (PDA)

- 8-15%
- this ductus contains specialized type of tissue which remains open by low O_2 concentration & certain pharmacological factors (e.g. prostaglandins)
- Normally it is closed within 24 Hrs after birth & anatomically it closes fully by 2 weeks to form ligamentum arteriosum.
- In those patients with PDA, the ductus become insensitive to O_2 or anti prostaglandins.
- In preterm babies, the ductus remains open for some time but it responds indomethacin (b/c it has normal tissue but decreased).

✓ **Pathophysiology & symptoms**

Blood shunt from aorta to pulmonary artery and will lead to same symptoms

✓ **Clinically**

- Vital signs. Wide pulse pressure (difference between systolic and diastolic > 15mmHg)
- Palmar pulse. (peculiar for PDA)
- Thrill over the base of the heart.
- Continuous murmur, systolic-diastolic murmur, or machinery murmur.
- Mid-diastolic rumble at the apex.

✓ **Investigations**

- chest X-Ray : cardiomegaly, lung congestion
- ECHO→ *diagnostic*

✓ **Management**

Very unlikely that PDA to close, so it is managed surgically:

- ligation →*preterm*
- By catheter: umbrella, coil →*older children*

(3) Atrial Septal Defect (ASD)

✓ **incidence**

- 8% of all CHD
- Female > Male
- 10% may be associated with mitral valve prolapse

✓ **Pathophysiology**

- Same

✓ **Symptoms**

- The least among Lt → Rt to cause symptoms
- Because of less Pr. Gradient between the two atria as compare to ventricles

✓ **Clinically**

- Bulging of chest wall (hypertrophy of Rt ventricle)
- Parasternal heave
- Normal S1, fixed splitting S2

- Ejection systolic murmur at pulmonary valve (relative Pul. stenosis
- Mid diastolic rumbling murmur at tricuspid valve
- On ECG → *right axis deviation*

Diagnosis: ECHO

✓ **Management**

- If the size < 3 cm it will close.
- If the size is large will not close

✓ **Complications**

1- may precipitate HF in females at 2nd or 3rd decades during pregnancy
2- arrhythmia (due to dilatation of Rt side of heart which contains conduction system)
3- pulmonary vascular disease
4- paradoxical thrombus formation

N.B. endocarditis rarely happens b/c the pressure gradient between Lt & Rt atria is not much high

(4) Endocardial Cushion Defect (ECD)

N.B. The medial leaflet of the tricuspid valve is inserted lower than the one of mitral valve normally

atrioventricular septum: it is the part of endocardium which consists of:

- the membranous portion of interventricular septum
- the atrioventricular septum (part of septum primum)
- the medial portion of tricuspid and mitral valves

it is also called

- atrioventricular septal defect
- atrial septal defect of septum primum
- AV common canal (the severest form)

✓ **Incidence**

The main lesion in babies born with trisomy 21 (50% of Down syndrome babies have CHD & of which 50% are ECD)

✓ **Pathophysiology**

- Lt → Rt shunt predominantly

- As the pressure ↑ *in pulmonary circulation, there is slight Rt* → Lt shunt. So, the blood O_2 saturation is slightly low than others.
- Patients start to develop symptoms between 6-8 weeks.

✓ **Symptoms**
- Same (Tachycardia, CHF)

✓ **Signs**
- vital signs nothing significant
- S1 normal, S2 fixed splitting
- VSD murmur: pansystolic murmur (left parasternal)

✓ **Investigations**
- CXR
- ECG Lt axis deviation
- ECHO: diagnostic

✓ **Management**
- Medical: only to contain symptoms, (HF, infection, feeding)
- Surgical: for Down syndrome send patient at 6 months – 1 year

✓ **Complications**
- infective endocarditis
- pulmonary vascular disease

(B) Obstructive lesions

⅄ **On the left side**
- Atresia of mitral valve
- Lt heart hypoplastic syndrome (Lt ventricle, MV, Aortic valve)
- Hypertrophic obstructive cardiomyopathy
- Subaortic membrane (SAM)
- Aortic valve stenosis
- Supra valvular aortic stenosis
- Coarctation of aorta

Coarctation of aorta برزخ الأورطي

✓ **Incidence**
- 4-6% of all CHD
- Known to be associated with Turner syndrome (20-30% of Pt with Turner have it)

✓ **Symptoms**

Depend on the severity of coarctation

Sever → heart failure during neonatal period

Moderate → detected on routine physical exam or follow up

✓ **Signs**
- Vital signs: BP on upper limp is > lower limp (>15 mmHg is significant)
- S1, S2 are normal
- Murmur may present over the back (interscapular area)

✓ **Investigations**
- CXR, ECG, ECHO→*Dx*

✓ **Management**
- Release the stenosis
- Ballon→*interventional cardiology*
- Surgery

✓ **Complications**
- Infective endocarditis
- Hypertension
- Heart failure

On the right side

Pulmonary Artery Stenosis

✓ **Incidence**
- 8-10% of all CHD

✓ **Symptoms**
- Dyspnea on exertion →*b/*c decrease pul. bl. flow
- Chest pain

✓ **Signs**
- bulging of the chest wall b/c of Rt Ventricular hypertrophy
- ejection systolic murmur best heard on Lt 2nd intercostal space

✓ **Investigations**
- CXR, ECG, ECHO→*Dx*

✓ **Management**
- Release the constriction either by:
  Ballooning
  Valvoplasty

✓ **Complications**
- Infective endocarditis

Cyanotic Heart Disease

- **with increase pulmonary blood flow**

In these lesions the patient will have the same symptoms of Lt→Rt shunt lesion except that he will be cyanosed (blue color) e.g.

- Total anomaly of pulmonary vein drainage
- Partial anomaly of pulmonary vein drainage(PAPVD)
- Truncus arteriosus
- Transposition of great arteries
- Single ventricle

- **with decreased pulmonary blood flow**
  - Tetralogy of Fallot
  - Tricuspid atresia
  - Pulmonary atresia
  - Ebstein anomaly of tricuspid valve

Tetralogy of Fallot

It consists of 4 components

1- Pulmonary stenosis (at valve or infundibulum)
2- Hypertrophy of Rt ventricle
3- VSD
4- Overriding of the aorta (displacement)

✓ **Incidence**

- 6-8% of all CHD
- The most common cyanotic lesion present beyond the 1st year of life

N.B. the sever the PS, the sever & early the presentation

✓ **Pathology**

- Sup. & Inf. Vena cava → Rt atrium → Rt ventricle →(PS, hypertrophy, overriding) aorta
- obstruction + Rt → Lt shunt

✓ **Presentation**

- Depend on the degree of PS

- sometimes they present with what is called hyper cyanotic spills (at 4-8 months) (excessive crying + cyanosis + tachypnea + loss of consciousness)

if these patients are disturbed $\xrightarrow{\uparrow \textit{adrenalin}}$ constriction of infundibulum → more PS

→ more cyanosis $\xrightarrow{\text{Low O2 to tissue}}$ hypoxia $\xrightarrow{\text{Anaerobic metabolism}}$ acidosis $\xrightarrow{\text{compensation}}$ tachypnea $\xrightarrow{\text{Low O2 to brain}}$ Loss of consciousness.

✓ **On examination**

- cyanosis
- finger & toe clubbing
- Rt precordial bulging
- S1 normal, single S2 (b/c PS)
- ESM
- squatting posture (ÎÝ Y ý ŎЧ ù) (to ↑ *pressure to aorta* → ↑ blood to lung)

✓ **Investigations**

- CXR heart size: boat shape sign, aortic arch to Rt
- Lung disease: like bronchiolitis, reduced vascularity
- ECG : Rt axis deviation
- ECHO→*Dx*
- CBC : polycythemia, microcytic hypochromic anemia (iron deficiency) → thrombosis

✓ **Management**

- There is no definite ttt but surgery

✓ **Complications**

1- Hypoxic spills. How to manage?
   - Put the child on chest knee position
   - Provide 100% O2
   - For acidosis give NaHCO3
   - To relax the infundibulum give B- blocker
   - To deal with irritability → morphine subcutaneously

2- Hyperviscosity syndrome → CVA

3- Brain abscess

Transposition of Great Arteries

D-transposition (switch of vessels)
L-transposition (switch of ventricles)

✓ **Pathophysiology**
- 2 separate circulations

✓ **Incidence**
- 4%

✓ **Signs & symptoms**
- more common in large babies (e.g. infants to diabetic mothers)
- cyanosis
- tachypnea

N.B. the site of murmur may not represent the site of the lesion

➢ **D.D. of baby discharged normally & represent again with the same picture**

1- Sepsis
2- CHD (TGA, hypoplastic Lt heart syndrome)
3- Inborn errors of metabolism

✓ **Investigations**
- CXR, ECG, ECHO

✓ **Management**

This is an emergency and the patient should have immediate intervention. (b/c the patient is ductus arteriosus dependant), so give prostaglandin & send the patient for early surgery.
- Surgery is done at 2 weeks before Lt ventricle gets small
- it is called switch surgery
- before they used to do major surgery

Good luck
Don' t forget to have fun

Your serenity
Mohammad Al-Dokhi
Hussain Al-Baharna
2006-12-01